

Best Available Copy

JAN

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: FONDA Examiner #: 71970 Date: 12-13-02
Art Unit: 1623 Phone Number 308-1620 Serial Number: 09759371
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL

8819 8A05
If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____
Inventors (please provide full names): _____
see attached assignment sheet

Earliest Priority Filing Date: 1-16-2001

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search compounds of claim 2 and methods of using them to treat inflammation or immune disorders. See claims 13, 14, and 16 for diseases. Administration can be oral, topical, intranasal, or by inhalation. All claims attached.

Thanks.

Kathleen

RUSH

I've asked Johann Richter to email authorization to you.

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

| STAFF USE ONLY | | Type of Search | Vendors and cost where applicable |
|--|---|---|-----------------------------------|
| Searcher: <u>Jan</u> | NA Sequence (#) _____ | STN <input checked="" type="checkbox"/> | |
| Searcher Phone #: <u>4498</u> | AA Sequence (#) _____ | Dialog _____ | |
| Searcher Location: _____ | Structure (#) <input checked="" type="checkbox"/> | Questel/Orbit _____ | |
| Date Searcher Picked Up: <u>12/15/02</u> | Bibliographic _____ | Dr. Link _____ | |
| Date Completed: <u>12/15/02</u> | Litigation _____ | Lexis/Nexis _____ | |
| Searcher Prep & Review Time: _____ | Fulltext _____ | Sequence Systems _____ | |
| Clerical Prep Time: <u>20</u> | Patent Family _____ | WWW/Internet _____ | |
| Online Time: <u>490</u> | Other _____ | Other (specify) _____ | |

82336
Delaval, Jan

From: Fonda, Kathleen
Sent: Saturday, December 14, 2002 10:27 AM
To: Delaval, Jan
Subject: 09/759,371

Hi Jan. Here are a few comments about 09/759,371 which I hope may streamline your job. Note that the compounds of claim 8 are not within the scope of claim 1, because claim 1 requires a glycoside. Also, US 20010041676 A1 is the patent pub that corresponds to my application. More than likely it has already been indexed by the folks at CA since it was published over a year ago. Thanks for your help. I will be here until 3 on Sat, in case you are in. Kathleen

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:28:31 ON 15 DEC 2002
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 13 DEC 2002 HIGHEST RN 476274-11-0
DICTIONARY FILE UPDATES: 13 DEC 2002 HIGHEST RN 476274-11-0

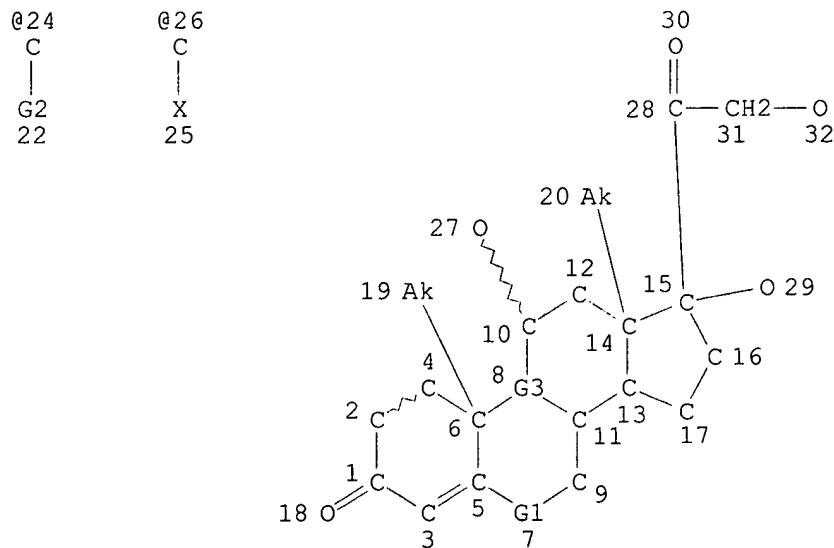
TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que 134
L12 STR



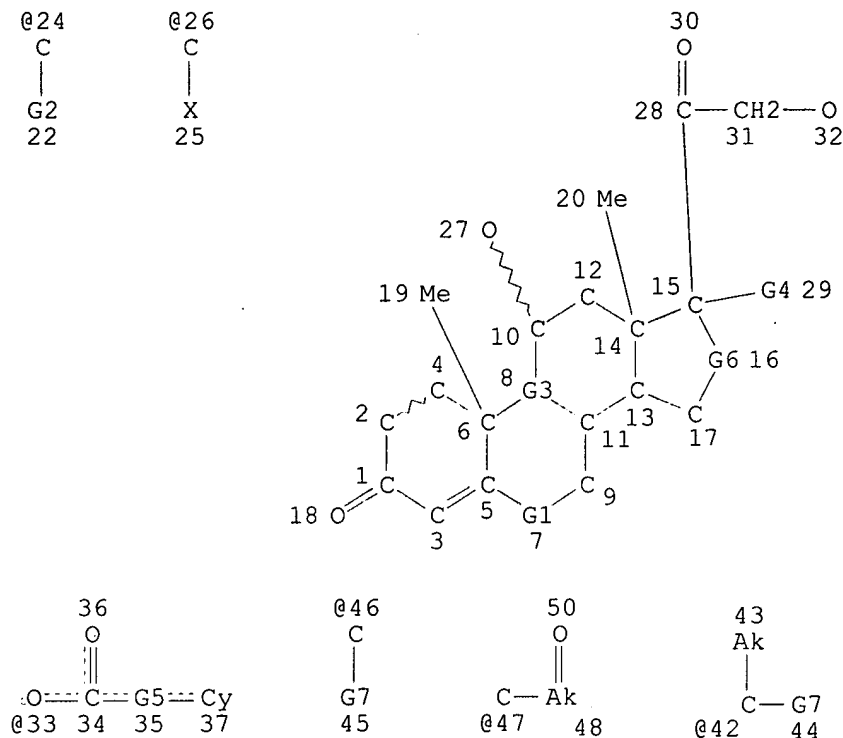
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CONNECT IS M1 RC AT 29
CONNECT IS M1 RC AT 32
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 iE07 - 703-308-4498
jan.delaval@uspto.gov

L14 5950 SEA FILE=REGISTRY CSS FUL L12
L15 STR



VAR G1=C/24
VAR G2=X/AK
VAR G3=C/26
VAR G4=OH/33
REP G5=(0-1) AK
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VAR G7=AK/OH
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 43

STEREO ATTRIBUTES: NONE

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L18 3 SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND OCOC2-OC5/ES
L19 131 SEA FILE=REGISTRY ABB=ON PLU=ON L17 AND 1/NC
L20 42 SEA FILE=REGISTRY ABB=ON PLU=ON L19 AND (N OR S OR P OR SI)/ELS
L21 17 SEA FILE=REGISTRY ABB=ON PLU=ON L20 AND (C41H57NO8 OR C37H54FNO12S OR C56H59NO19 OR C43H66FNO12S OR C34H49FO11S OR C40H55NO8 OR C40H60FNO12S OR C68H109FN6O26S3 OR C43H66FNO12S OR C63H63NO21 OR C39H58FNO12S OR C35H51NO10 OR C40H60FNO12S OR C61H95FN4O25S3 OR C36H52FNO12S OR C40H60FNO12S OR C37H55FO11S)
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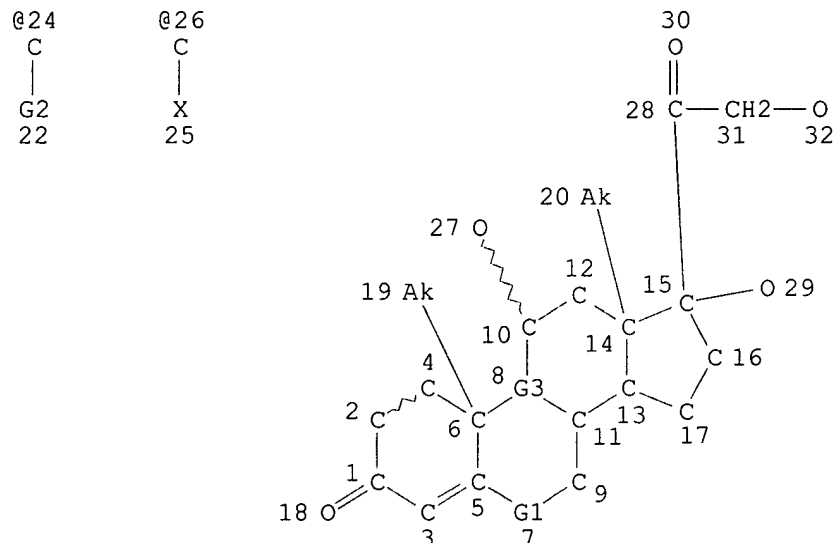
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L34      124 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L26 OR L31 OR L33)

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=> d sta que 144

L12 STR



VAR G1=C/24

VAR G2=X/AK

VAR G3=C/26

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 16

CONNECT IS M1 RC AT 29

CONNECT IS M1 RC AT 32

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

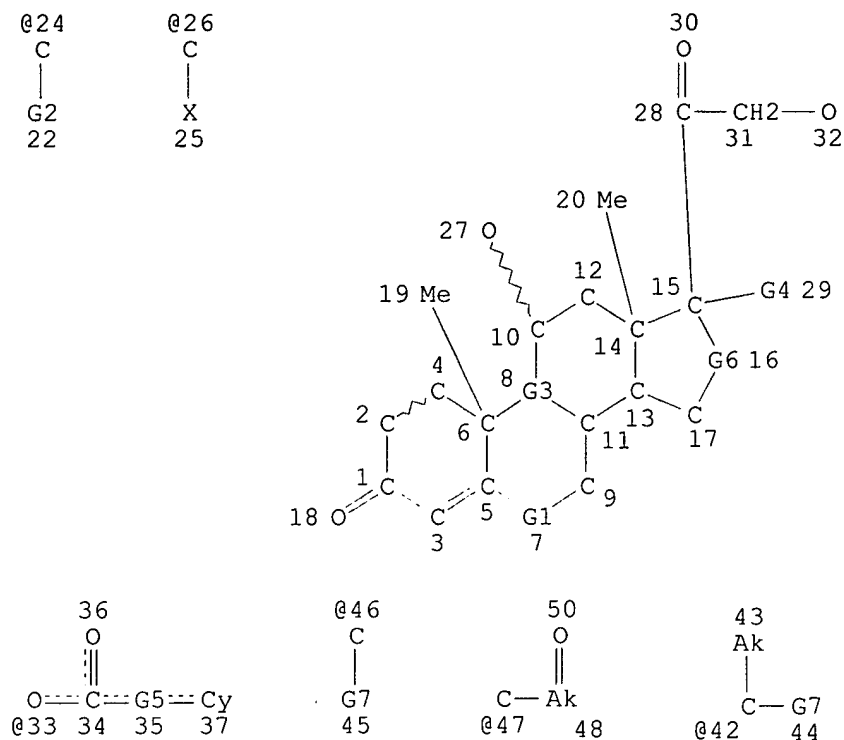
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STEREO ATTRIBUTES: NONE

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L15 STR



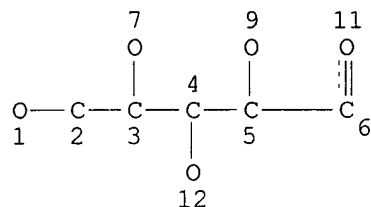
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 REP G5=(0-1) AK
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 CONNECT IS M1 RC AT 32
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 43

STEREO ATTRIBUTES: NONE

L16 3653 SEA FILE=REGISTRY SUB=L14 CSS FUL L15
 L17 227 SEA FILE=REGISTRY ABB=ON PLU=ON L16 AND OC5/ES
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 L19 131 SEA FILE=REGISTRY ABB=ON PLU=ON L17 AND 1/NC
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 SI)/ELS
 L21 17 SEA FILE=REGISTRY ABB=ON PLU=ON L20 AND (C41H57NO8 OR
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 OR C63H63NO21 OR C39H58FNO12S OR C35H51NO10 OR C40H60FNO12S OR
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 L22 25 SEA FILE=REGISTRY ABB=ON PLU=ON L20 NOT L21
 L23 89 SEA FILE=REGISTRY ABB=ON PLU=ON L19 NOT L20
 L24 19 SEA FILE=REGISTRY ABB=ON PLU=ON L23 AND (C30H39FO8 OR
 C28H36O8 OR C26H37FO6 OR C26H38O6 OR C26H36O6 OR C30H38F2O8 OR
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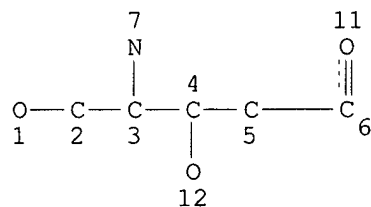
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 DEFAULT ECLEVEL IS LIMITED

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 NUMBER OF NODES IS 10

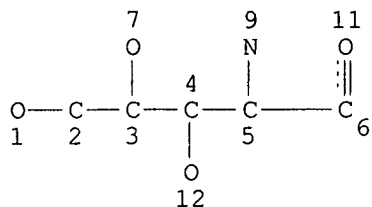
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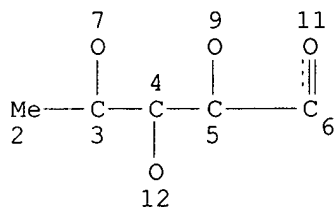
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NODE ATTRIBUTES:
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 NUMBER OF NODES IS 10

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NODE ATTRIBUTES:
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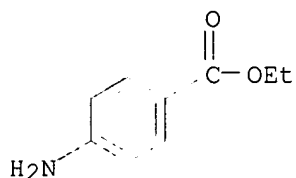
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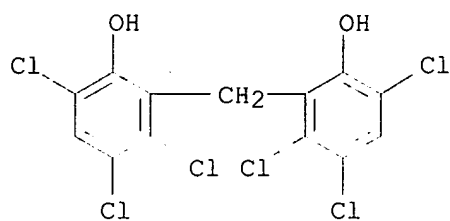
=> d scan l44

L44 3 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN Meripons (8CI)
 MF C23 H32 O6 . C17 H22 N2 O . C13 H6 Cl6 O2 . C9 H13 N O2 . C9 H11 N O2 . C6
 H12 O6 . C4 H6 O4 . Cl H
 CI MXS

CM 1

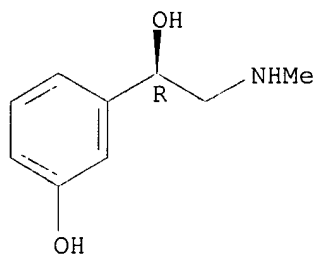


CM 2



CM 3

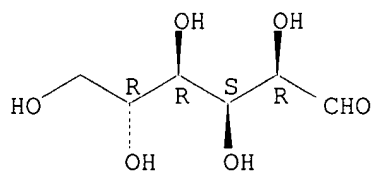
Absolute stereochemistry.



● HCl

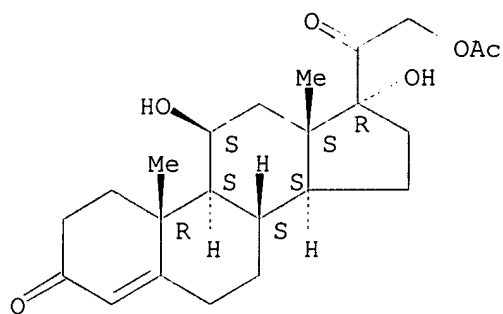
CM 4

Absolute stereochemistry.



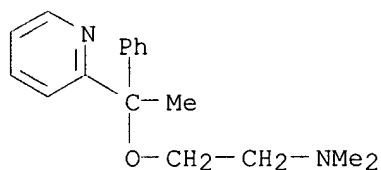
CM 5

Absolute stereochemistry.

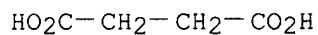


CM 6

CM 7



CM 8



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):

L44 3 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Heparin, mixt. with D-glucose and (11.beta.)-11,17,21-trihydroxypregn-4-ene-3,20-dione (9CI)

MF C21 H30 O5 . C6 H12 O6 . Unspecified

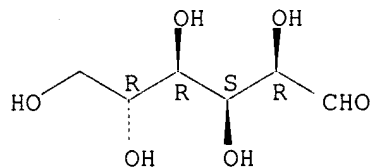
CI MXS

CM 1

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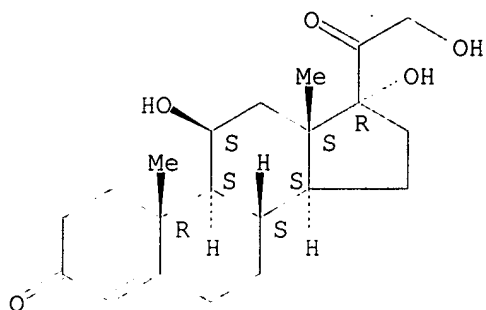
CM 2

Absolute stereochemistry.



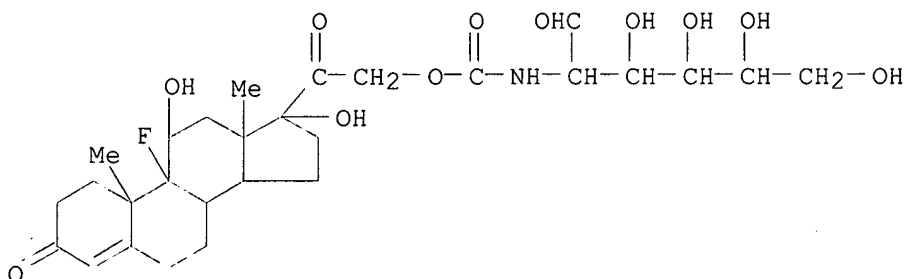
CM 3

Absolute stereochemistry.



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):

L44 3 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN D-Glucose, 2-deoxy-2-[[[(11.beta.)-9-fluoro-11,17-dihydroxy-3,20-dioxopregn-4-en-21-yl]oxy]carbonyl]amino]- (9CI)
 MF C28 H40 F N O11



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> d his

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 SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:09:20 ON 15 DEC 2002

| | |
|----|--------------------------------|
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| L1 | 11 S E3-E10 |
| | E HOLICK M/AU |
| L2 | 475 S E3-E11 |
| | E RAMANATHAN H/AU |
| L3 | 22 S E3,E4 |
| L4 | 6 S L1 AND L2,L3 |
| L5 | 22 S L1-L3 AND STEROID?/SC, SX |
| L6 | 4 S L5 NOT ?VITAMIN? |
| | E US2001-41676/AP, PRN |
| | E US2001041676/PN |
| L7 | 1 S E3 |

L8 1 S L7 AND L1-L7
SEL RN

FILE 'REGISTRY' ENTERED AT 13:13:29 ON 15 DEC 2002

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L10 5 S L9 AND NR>=5
L11 4 S L10 NOT C24H31FO6
L12 STR
L13 50 S L12 CSS
L14 5950 S L12 CSS FUL
SAV L14 FONDA759/A
L15 STR L12
L16 3653 S L15 CSS FUL SUB=L14
SAV L16 FONDA759A/A
L17 227 S L16 AND OC5/ES
L18 3 S L16 AND OCOC2-OC5/ES
L19 131 S L17 AND 1/NC
L20 42 S L19 AND (N OR S OR P OR SI)/ELS
L21 17 S L20 AND (C41H57NO8 OR C37H54FNO12S OR C56H59NO19 OR C43H66FNO
L22 25 S L20 NOT L21
L23 89 S L19 NOT L20
L24 19 S L23 AND (C30H39FO8 OR C28H36O8 OR C26H37FO6 OR C26H38O6 OR C2
L25 70 S L23 NOT L24
L26 98 S L18,L22,L25
L27 95 S L16 AND OC4/ES
L28 44 S L27 AND NC>=2
L29 51 S L27 NOT L28
L30 96 S L17 NOT L19
L31 5 S L30 AND (H3N OR BA/ELS OR H2O)
L32 23 S L30 AND NA/ELS
L33 21 S L32 NOT (MXS/CI OR C29H38O8)
L34 124 S L26,L31,L33
L35 3344 S L16 NOT L17-L34
L36 STR
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L38 STR L36
L39 0 S L38 FUL SUB=L35
L40 STR L36
L41 1 S L40 FUL SUB=L35
L42 STR L36
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SAV L44 FONDA759B/A
SAV L34 FONDA759C/A

FILE 'HCAOLD' ENTERED AT 14:01:06 ON 15 DEC 2002

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L46 0 S L11
SEL AN L45
EDIT E14-E30
EDIT E14-E30 /AN /OREF

FILE 'HCAPLUS' ENTERED AT 14:02:31 ON 15 DEC 2002

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SEL DN 3 5 7 9 11 14 17 19 21 22 24 26
L48 12 S L47 AND E31-E42
SEL DN 8
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L51 17 S L47 NOT L50
L52 6 S L11
L53 50 S L34
L54 50 S L52,L53

L55 1 S L54 AND L1-L3
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L57 49 S L54 NOT L55
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L59 17 S L54 AND (?INFLAM? OR IMMUN?(L)RESPON? OR ADRENAL(L)INSUFF? OR
E ADREN/CT
L60 2998 S E10-E21
E E9+ALL
L61 29468 S E3+NT
E E8+ALL
L62 6512 S E3+NT
E ADDISON/CT
L63 460 S E5
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L64 460 S E5+NT
E CONGENITAL HYPERPLASIA/CT
E E4+ALL
L65 341 S E2
E INFLAMMATION/CT
L66 23441 S E3-E18
E E3+ALL
L67 71073 S E2+NT
L68 10697 S E37+NT
E E36+ALL
L69 47496 S E4, E5, E3+NT
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 E E4+ALL
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L92 9 S L54 AND L60-L91
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L97 30 S L54 NOT L96
L98 27 S L97 NOT L51
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L100 24 S L96,L99
L101 13 S L51 NOT L100
L102 1 S L101 AND ALLERG?
L103 25 S L100,L102
L104 35 S L51,L54 NOT L103
 SAV L104 FONDA759D/A

FILE 'REGISTRY' ENTERED AT 14:28:31 ON 15 DEC 2002

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 14:29:18 ON 15 DEC 2002

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FILE COVERS 1907 - 15 Dec 2002 VOL 137 ISS 25

FILE LAST UPDATED: 13 Dec 2002 (20021213/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l103 all hitstr tot

L103 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:525925 HCAPLUS

DN 135:102902

TI Synthesis of glycosides and orthoester glycosides of glucocorticoids and

uses of in therapy

IN **Holick, Michael Francis; Ramanathan, Halasya**

PA **Strakan Group PLC, UK**

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-575

ICS A61P029-00

CC 2-4 (Mammalian Hormones)

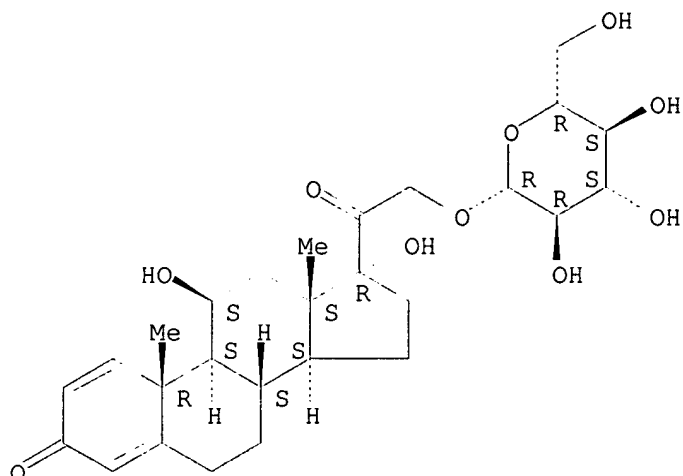
Section cross-reference(s): 32, 33

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|--|----------|-----------------|--------------|
| PI | WO 2001051057 | A2 | 20010719 | WO 2001-GB146 | 20010115 <-- |
| | WO 2001051057 | A3 | 20020321 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2001041676 | A1 | 20011115 | US 2001-759371 | 20010116 <-- |
| PRAI | US 2000-176007P | P | 20000114 | <-- | |
| OS | MARPAT 135:102902 | | | | |
| AB | Serum levels of therapeutically useful glucocorticosteroids are substantially increased by oral administration of the corresponding glycoside or orthoester glycoside. In one aspect, the present invention provides a compn. for the treatment of a condition treatable by the systemic administration of a glucocorticosteroid, characterized in that the glucocorticosteroid is a deriv. in the form of a glycoside or orthoester glycoside, or salt or ester of the deriv. In another aspect, the invention relates to use of the glycosides and orthoester glycosides in therapy, esp. in the treatment of such conditions as adrenal insufficiency, inflammation and the modulation of immune responses . | | | | |
| ST | glycoside glucocorticoid prepn therapeutic use | | | | |
| IT | Blood analysis | | | | |
| | HPLC | | | | |
| | (HPLC assay of prednisolone and prednisolone glucoside in blood serum) | | | | |
| IT | Adrenal cortex, disease | | | | |
| | (congenital adrenal hyperplasia; | | | | |
| | synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy) | | | | |
| IT | Brain, disease | | | | |
| | (edema; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy) | | | | |
| IT | Glucocorticoids | | | | |
| | RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) | | | | |
| | (glycosides and orthoester glycosides; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy) | | | | |
| IT | Development, mammalian postnatal | | | | |
| | (infant, infantile massive spasm ; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy) | | | | |
| IT | Convulsion | | | | |
| | (infantile massive spasm ; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy) | | | | |

- IT **Eye, disease**
(inflammation; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT **Adrenal gland, disease**
(insufficiency; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT **Kidney, disease**
(nephrotic syndrome; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT **Respiratory distress syndrome**
(newborn; synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT **Addison's disease**
Allergy inhibitors
Anti-inflammatory agents
Antiarthritics
Anticonvulsants
Antirheumatic agents
Immunomodulators
Skin, disease
(synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT Drug delivery systems
(therapeutic compns. contg. glycosides and orthoester glycosides of glucocorticoids)
- IT 50-02-2DP, Dexamethasone, glycosides and orthoester glycosides
50-23-7DP, Hydrocortisone, glycosides and orthoester glycosides
50-24-8DP, Prednisolone, glycosides and orthoester glycosides 53-03-2DP,
Prednisone, glycosides and orthoester glycosides 76-25-5DP,
Triamcinolone acetonide, glycosides and orthoester glycosides 83-43-2DP,
Methylprednisolone, glycosides and orthoester glycosides 378-44-9DP,
Betamethasone, glycosides and orthoester glycosides 88158-44-5P,
Prednisolone glucoside 350610-18-3P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT 50-24-8, Prednisolone 53-03-2, Prednisone 572-09-8, Acetobromoglucose 42613-24-1, Silver silicate
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT 88179-95-7P, Prednisolone-21-O-glucoside tetraacetate 350610-17-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- IT 88158-44-5P, Prednisolone glucoside 350610-18-3P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)
- RN 88158-44-5 HCAPLUS
- CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

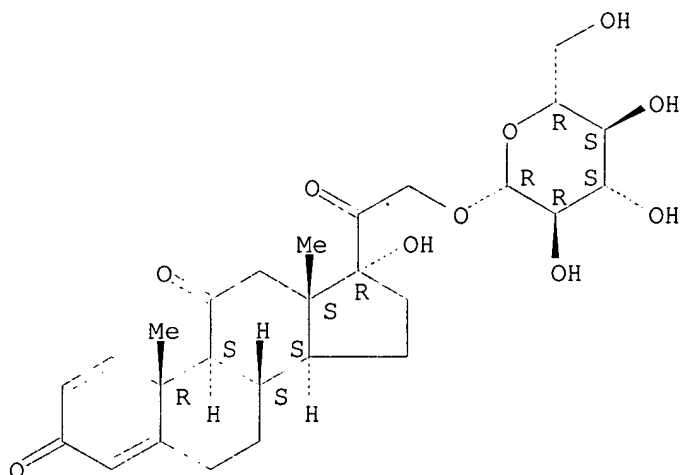
Absolute stereochemistry.



RN 350610-18-3 HCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 21-(.beta.-D-glucopyranosyloxy)-17-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 88179-95-7P, Prednisolone-21-O-glucoside tetraacetate
350610-17-2P

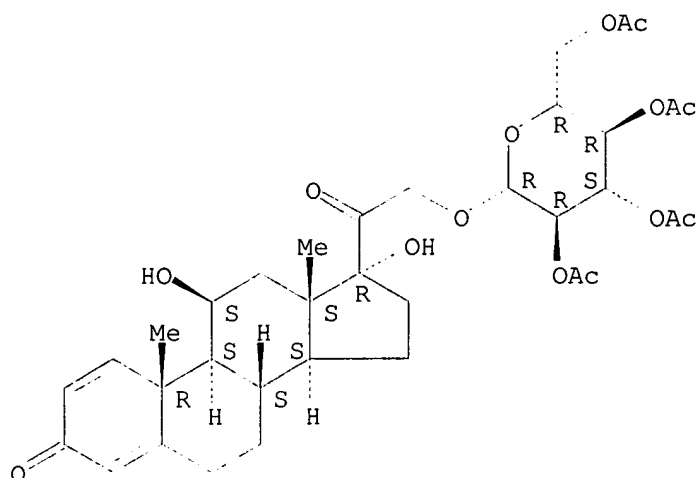
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of glycosides and orthoester glycosides of glucocorticoids and uses of in therapy)

RN 88179-95-7 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

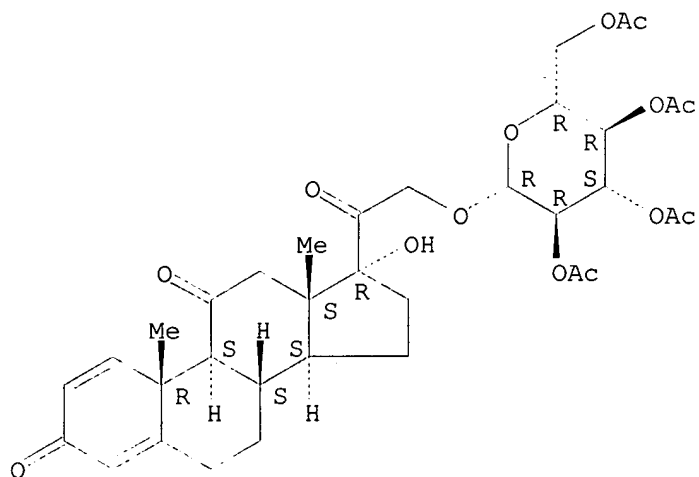
Absolute stereochemistry.



RN 350610-17-2 HCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 17-hydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:31363 HCAPLUS

DN 134:95484

TI Compositions and methods for targeted enzymic release of cell regulatory compounds

IN Naleway, John; Howard, Rachel

PA Marker Gene Technologies, Inc., USA

SO PCT Int. Appl., 97 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K048-00

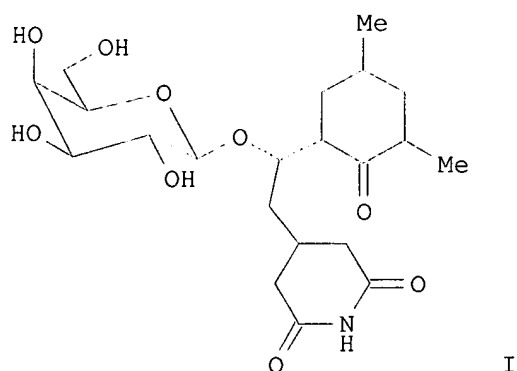
CC 1-6 (Pharmacology)

Section cross-reference(s): 33, 63

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

PI WO 2001002020 A2 20010111 WO 2000-US15156 20000601 <--
 WO 2001002020 A3 20010719
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
 CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
 ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
 LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
 SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
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 EP 1200131 A2 20020502 EP 2000-946772 20000601 <--
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 SI, LT, LV, FI, RO, MK, CY, AL
 PRAI US 1999-343325 A2 19990630 <--
 WO 2000-US15156 W 20000601 <--
 GI



AB Novel prodrugs and methods for their use to alter the growth and biol. characteristics of living cells, tissues, or whole organisms are described. The methods allow for selective activation of the prodrugs at or near transformant host cells expressing a gene for an enzyme that activates the pro-drugs. Prodrugs according to a preferred embodiment of the invention are conjugates of a bioactive compd. and a chem. group that is capable of being cleaved from the bioactive compd. by action of an enzyme. Methods according to this invention include: (a) introducing into targeted cells a gene encoding an enzyme and (b) administering a prodrug, wherein the enzyme releases the prodrug from conjugation. In a preferred embodiment of the invention, the gene encoding the enzyme is a marker gene. A 5-fluorouridine 5'-O-.beta.-D-galactoside conjugate (I) was prepd.

ST prodrug conjugate prepn targeted enzymic release

IT Gene, animal
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (-encoding enzyme; compns. and methods for targeted enzymic release of cell regulatory compds.)

IT Antitumor agents
 Drug targeting
 Escherichia coli
 (compns. and methods for targeted enzymic release of cell regulatory compds.)

IT Enzymes, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compns. and methods for targeted enzymic release of cell regulatory

compsd.)

IT Gene, microbial
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lacZ; compns. and methods for targeted enzymic release of cell regulatory compds.)

IT Photinus pyralis
Renilla reniformis
(luciferase of; compns. and methods for targeted enzymic release of cell regulatory compds.)

IT Drug delivery systems
(prodrugs; compns. and methods for targeted enzymic release of cell regulatory compds.)

IT 9001-45-0, .beta.-Glucuronidase 9001-78-9 9031-11-2,
.beta.-Galactosidase 9073-60-3, .beta.-Lactamase 61869-41-8,
Luciferase 61970-00-1, Luciferase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(compns. and methods for targeted enzymic release of cell regulatory compds.)

IT 88337-91-1P 149965-92-4P 191476-32-1P 319426-55-6P
319426-57-8P 319426-59-0P 319426-63-6P 319426-65-8P
319426-67-0P 319426-69-2P 319426-70-5P 319426-71-6P 319426-72-7P
319426-73-8P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(compns. and methods for targeted enzymic release of cell regulatory compds.)

IT 50-02-2, Dexamethasone 50-89-5, Thymidine, reactions 56-75-7,
Chloramphenicol 56-81-5, Glycerol, reactions 60-54-8, Tetracycline
66-81-9, Cycloheximide 111-64-8, Octanoyl chloride 302-79-4, Retinoic
acid 316-46-1, 5-Fluorouridine 369-07-3, 2-Nitrophenyl
.beta.-D-galactopyranoside 501-36-0, Resveratrol 939-69-5,
2-Cyano-6-hydroxybenzothiazole 957-68-6, 7-Aminocephalosporanic acid
3068-32-4, Acetobromogalactose 3150-24-1 3695-77-0,
Triphenylmethylmercaptan 4761-00-6, 2,4,6-Trimethylbenzyl bromide
5328-37-0, L-Arabinose 13726-84-6 17673-25-5, Phorbol 23214-92-8,
Doxorubicin 70476-82-3, Mitoxantrone dihydrochloride 77813-95-7
261508-68-3 319426-83-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(compns. and methods for targeted enzymic release of cell regulatory compds.)

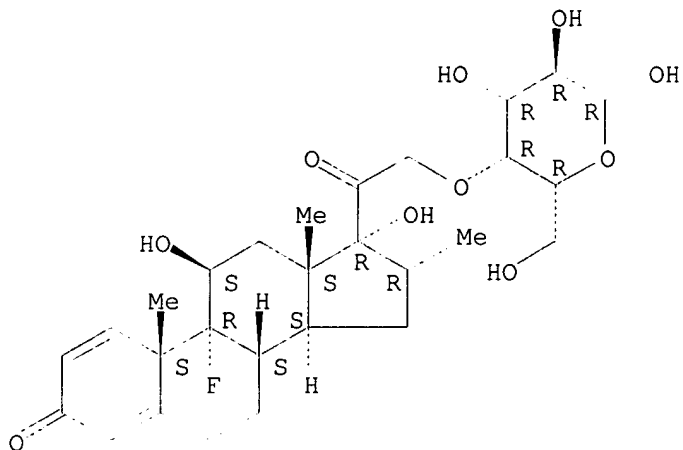
IT 100-79-8P 859-07-4P 1069-87-0P 2797-17-3P 4799-67-1P 5094-33-7P,
4-Aminophenyl .beta.-D-galactopyranoside 15028-56-5P 41128-81-8P
62442-59-5P 88824-10-6P 145827-12-9P 319426-74-9P 319426-75-0P
319426-76-1P 319426-77-2P 319426-78-3P 319426-79-4P 319426-80-7P
319426-81-8P 319426-82-9P 319426-84-1P 319426-85-2P 319426-86-3P
319426-87-4P 319426-88-5P 319426-89-6P 319426-90-9P 319426-91-0P
319426-92-1P 319426-93-2P 319426-94-3P 319426-95-4P 319426-96-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(compns. and methods for targeted enzymic release of cell regulatory compds.)

IT 319426-57-8P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(compns. and methods for targeted enzymic release of cell regulatory compds.)

RN 319426-57-8 HCAPLUS

CN .beta.-D-Galactopyranose, 4-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:727481 HCAPLUS

DN 128:66372

TI Steady-state pharmacokinetics of corticosteroid delivery from glucuronide prodrugs in normal and colitic rats

AU Nolen, Harold W., III; Fedorak, Richard N.; Friend, David R.

CS Pharmaceutical Formulation Design Group, SRI International, Menlo Park, CA, 94025, USA

SO Biopharmaceutics & Drug Disposition (1997), 18(8), 681-695

CODEN: BDDID8; ISSN: 0142-2782

PB Wiley

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 2

AB Ulcerative colitis and Crohn's colitis are chronic intestinal diseases usually treated with various nonsteroidal **antiinflammatory** agents to maintain remission. Corticosteroids, while useful in acute treatment of these diseases, present side-effects generally too serious to allow maintenance therapy. Colon-specific drug delivery may permit use of corticosteroids for maintenance therapy if doses can be reduced while maintaining efficacy. In this study, two prodrugs (dexamethasone-.beta.-D-glucuronide (DXglrd) and budesonide-.beta.-D-glucuronide (BUDglrd)) were administered by intragastric (ig) infusion to conventional and colitic rats. In addn., dexamethasone (DX) and budesonide (BUD) were administered with ig or s.c. to healthy and colitic rats. Colon-specific delivery was assessed using the drug delivery index (DDI). In conventional rats, DDIs for DXglrd ranged from about five to as high as 11 in the luminal contents relative to DX administered s.c. or ig. DDI values were also elevated in the mucosa of both healthy and colitic rats following ig administration of DXglrd. BUD was delivered somewhat less effectively from BUDglrd to the rat large intestine than was DX and DXglrd. The data are consistent with efficacy studies and support the conclusion that local delivery of corticosteroids to the large intestine is due, at least in part, to higher levels of drug delivery into the mucosal tissues.

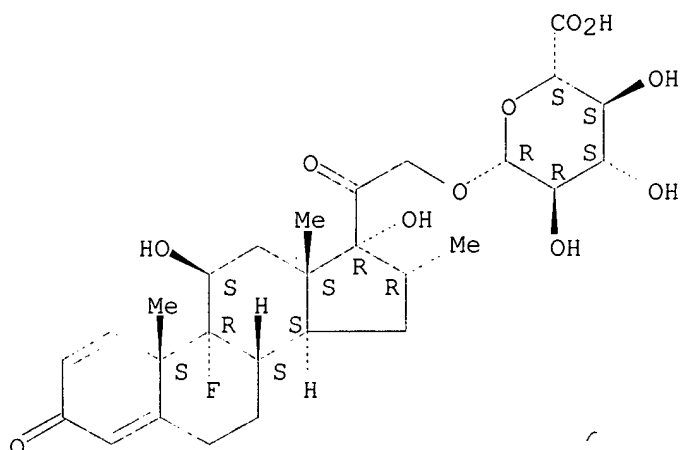
ST corticosteroid prodrug delivery Crohn disease

IT Intestine, disease

(Crohn's; steady-state pharmacokinetics of corticosteroid delivery from

- glucuronide prodrugs in normal and colitic rats)
- IT Drug delivery systems
(prodrugs; steady-state pharmacokinetics of corticosteroid delivery from glucuronide prodrugs in normal and colitic rats)
- IT Drug delivery systems
Pharmacokinetics
(steady-state pharmacokinetics of corticosteroid delivery from glucuronide prodrugs in normal and colitic rats)
- IT Corticosteroids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(steady-state pharmacokinetics of corticosteroid delivery from glucuronide prodrugs in normal and colitic rats)
- IT 152129-70-9, Budesonide-.beta.-D-glucuronide 152154-28-4, Dexamethasone-.beta.-D-glucuronide
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(steady-state pharmacokinetics of corticosteroid delivery from glucuronide prodrugs in normal and colitic rats)
- IT 152154-28-4, Dexamethasone-.beta.-D-glucuronide
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(steady-state pharmacokinetics of corticosteroid delivery from glucuronide prodrugs in normal and colitic rats)
- RN 152154-28-4 HCAPLUS
- CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:521733 HCAPLUS

DN 125:230346

TI Glucuronide prodrugs for colonic delivery: steady-state kinetics in conventional and colitic rats

AU Nolen, H. III; Fedorak, R. N.; Friend, D. R.

CS Controlled Release Department, SRI International, Menlo Park, CA, 94025, USA

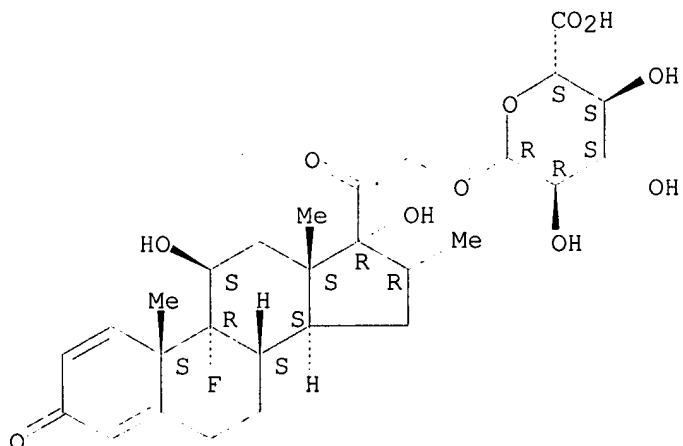
SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1996), 23rd, 61-62

CODEN: PCRMEY; ISSN: 1022-0178

PB Controlled Release Society, Inc.

DT Journal
 LA English
 CC 63-5 (Pharmaceuticals)
 AB Two prodrugs of dexamethasone-.beta.-D-glucuronide (I) and budesonide-.beta.-D-glucuronide (II) were administered by intragastric infusion to conventional rats and colitis rats. All animals then were infused for a sufficient time to achieve steady-state in plasma and gastrointestinal tissue and a drug delivery index was calcd. Both I and II delivered more of their resp. drugs to the mucosa of the rat large intestine than was possible from conventional dosing of these drugs.
 ST steroid glucuronide prodrug colonic delivery colitis
 IT Steroids, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 IT Intestine, disease (colitis, glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 IT Intestine, disease (inflammatory, glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 IT Pharmaceutical dosage forms (prodrugs, glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 IT 152154-28-4P, Dexamethasone-.beta.-D-glucuronide
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 IT 152129-70-9, Budesonide-.beta.-D-glucuronide
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 IT 152154-28-4P, Dexamethasone-.beta.-D-glucuronide
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (glucuronide prodrugs of steroids for colonic delivery in colitic rats)
 RN 152154-28-4 HCAPLUS
 CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:881298 HCAPLUS

DN 123:286523

TI Preparation of 21-monosaccharide substituted steroid compounds as
antiinflammatory agentsIN Sugai, Kei; Goto, Motoaki; Yoshida, Satoshi; Okuno, Yumiko; Ishii,
Takayuki; Kibushi, Nobuyuki; Nishikawa, Hutoshi

PA Mect Corp., Japan

SO PCT Int. Appl., 139 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

IC ICM C07J017-00

ICS A61K031-705

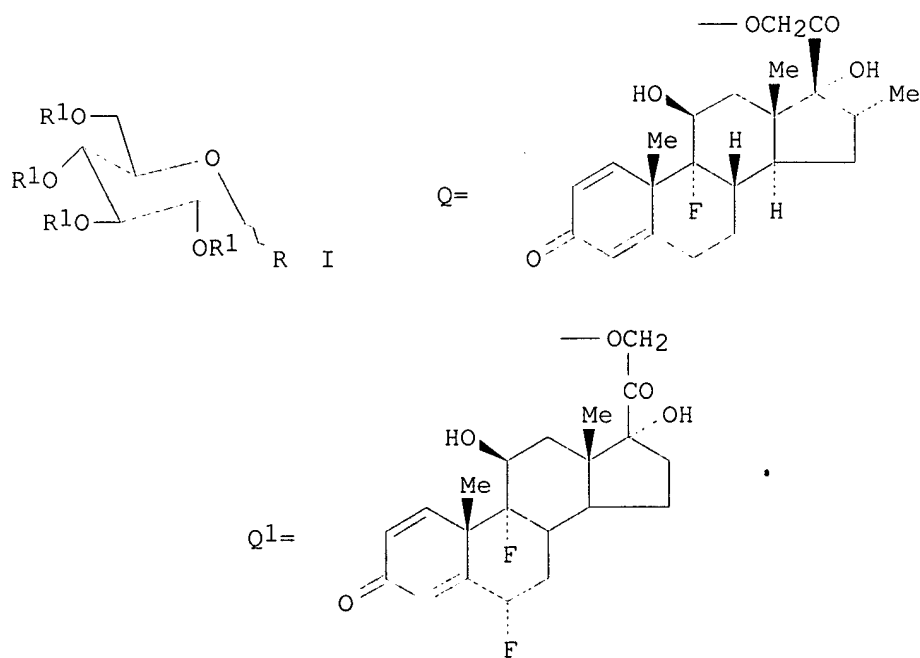
CC 33-8 (Carbohydrates)

Section cross-reference(s): 1

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|------|---|------|----------|-----------------|----------|-----|
| PI | WO 9509177 | A1 | 19950406 | WO 1994-JP1602 | 19940928 | <-- |
| | W: CA, JP, US | | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | | |
| | CA 2172983 | AA | 19950406 | CA 1994-2172983 | 19940928 | <-- |
| | EP 721956 | A1 | 19960717 | EP 1994-927793 | 19940928 | <-- |
| | EP 721956 | B1 | 20000802 | | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| | AT 195127 | E | 20000815 | AT 1994-927793 | 19940928 | <-- |
| | US 5945404 | A | 19990831 | US 1997-927399 | 19970910 | <-- |
| PRAI | JP 1993-243123 | A | 19930929 | | | <-- |
| | WO 1994-JP1602 | W | 19940928 | | | <-- |

GI



AB A steroid glycoside (wherein the 21-position of the steroid is substituted by a monosaccharide or an acylated sugar selected from glucose, galactose,

mannose, rhamnose, fucose, N-acetylglucosamine, N-acetylgalactosamine, galacturonic acid, glucuronic acid and sialic acid) is prepd. The hydroxy groups of the acylated sugar are protected by toluoyl, benzoyl, p-chlorobenzoyl, or arylalkyl. The preferred steroid is difluprednate, diflorasone, diflucortolone, dexamethasone, betamethasone, or betamethasone valerate. This glycoside shows reduced side effects since it is resistant to common glycosidase and is converted into active steroid by glycosidase increased at **inflammation** sites. Thus, 300 mg dexamethasone was glycosidated with 1.10 g per(p-toluoyl)-.alpha.-D-glucopyranosyl bromide in the presence of silver triflate and mol. sieve 5A in THF at room temp. for 2 h to give, after silica gel chromatog. and reversed phase HPLC, 32.3% .beta.-D-glucopyranosyldexamethasone (I; R = .beta.-Q, R1 = toluoyl) and 6.7% .alpha.-anomer I (R = .alpha.-Q, R1 = toluoyl), which were treated with NaOMe in MeOH at room temp. for 5 h to give, after HPLC purifn., .beta.-glycoside I (R = .beta.-Q, R1 = H) (II) and .alpha.-glycoside (R = .alpha.-Q, R1 = H) in 88.5 and 40.0%, resp. In paper disk assay, II in vivo decreased granuloma in rats by 47.4% compared to the control. .beta.-D-Glucopyranosyldifluprednate I (R = .beta.-Q1, R1 = H) at 1.0 mg inhibited the croton oil-induced granuloma in rats by 76.4+-.4.3%. A vaseline-based ointment (0.1% equiv. dexamethasone, 20 mg) contg. acetylated .beta.-D-glucopyranosyldexamethasone I (R = .beta.-Q, R1 = Ac), which was applied to the right ear of mice, inhibited the croton oil-induced ear edema by 49.8+-.9.7%.

ST monosaccharide glycoside steroid prepn **antiinflammatory**;

granuloma treatment steroid glycoside; edema treatment steroid glycoside

IT **Inflammation inhibitors**

(prepn. of monosaccharide-substituted steroid compds. as **antiinflammatory** agents)

IT Glycosides

Steroids, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of monosaccharide-substituted steroid compds. as **antiinflammatory** agents)

IT Edema

Granuloma

(prepn. of monosaccharide-substituted steroid compds. as **antiinflammatory** agents for treating granuloma and edema)

IT **169454-05-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(intermediate for prepn. of monosaccharide-substituted steroid compds. as **antiinflammatory** agents)

IT 572-09-8P, 2,3,4,6-Tetra-O-acetyl-.alpha.-D-glucopyranosyl bromide
3068-34-6P, N,3,4,6-O-Tetraacetyl-.alpha.-D-glucosaminyl chloride
4163-65-9P, 1,2,3,4,6-Penta-O-acetyl-.alpha.-D-mannopyranose 7355-18-2P
13242-53-0P 13350-45-3P 14218-11-2P 21085-72-3P 22415-91-4P
41355-44-6P, N,3,4,6-O-Tetraacetyl-.alpha.-D-galactosaminyl chloride
56768-32-2P 64913-16-2P, 1,2,3,4-Tetra-O-acetyl-.alpha.-L-fucopyranose
84635-54-1P 100083-77-0P 100102-39-4P 104992-64-5P 110797-45-0P
114853-37-1P 153215-00-0P 153215-01-1P 157848-88-9P 169453-92-3P
169453-93-4P 169453-94-5P 169453-95-6P 169453-96-7P
169453-97-8P 169453-98-9P 169453-99-0P 169454-00-6P
169454-01-7P 169454-02-8P 169454-04-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate for prepn. of monosaccharide-substituted steroid compds. as **antiinflammatory** agents)

IT **4157-53-3P 6804-44-0P 88158-43-4P**
88158-45-6P 92901-23-0P 92901-30-9P

152154-28-4P 153247-83-7P 153247-84-8P
153247-87-1P 169453-45-6P 169453-46-7P
169453-47-8P 169453-48-9P 169453-49-0P
169453-50-3P 169453-51-4P 169453-52-5P
169453-53-6P 169453-54-7P 169453-55-8P
169453-56-9P 169453-57-0P 169453-58-1P
169453-59-2P 169453-60-5P 169453-61-6P 169453-62-7P
169453-63-8P 169453-64-9P 169453-65-0P
169453-66-1P 169453-67-2P 169453-68-3P
169453-69-4P 169453-70-7P 169453-71-8P
169453-72-9P 169453-73-0P 169453-74-1P
169453-75-2P 169453-76-3P 169453-77-4P
169453-78-5P 169453-79-6P 169453-80-9P
169453-81-0P 169453-82-1P 169453-83-2P
169453-84-3P 169453-85-4P 169453-86-5P 169453-87-6P 169453-88-7P
169453-89-8P 169453-90-1P 169453-91-2P
169454-03-9P

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(prepn. of monosaccharide-substituted steroid compds. as
antiinflammatory agents)

IT 50-02-2, Dexamethasone 50-99-7, D-Glucose, reactions 59-23-4,
D-Galactose, reactions 75-36-5, Acetyl chloride 98-88-4, Benzoyl
chloride 108-24-7, Acetic anhydride 122-01-0, p-Chlorobenzoyl chloride
334-88-3, Diazomethane 378-44-9, Betamethasone 604-69-3,
1,2,3,4,6-Penta-O-acetyl-.beta.-D-glucopyranose 685-73-4, D-Galacturonic
acid 806-29-1 874-60-2, p-Toluoyl chloride 933-88-0, o-Toluoyl
chloride 1711-06-4, m-Toluoyl chloride 1811-31-0, N-Acetyl-D-
galactosamine 2152-44-5, Betamethasone valerate 2438-80-4, L-Fucose
2557-49-5, Diflorasone 2607-06-9, Diflucortolone 3458-28-4, D-Mannose
7512-17-6, N-Acetyl-D-glucosamine 17314-32-8, Tributyltin methyl sulfide
18281-92-0 67670-69-3 110224-78-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of monosaccharide-substituted steroid compds. as
antiinflammatory agents)

IT 169454-05-1P

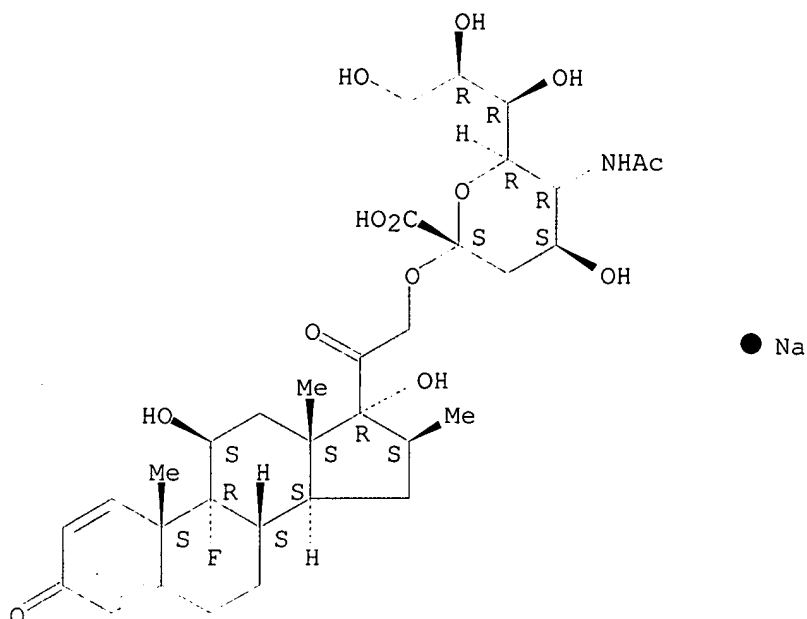
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(intermediate for prepn. of monosaccharide-substituted steroid compds.
as antiinflammatory agents)

RN 169454-05-1 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.beta.)-9-fluoro-11,17-
dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, monosodium salt
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 169453-97-8P 169453-98-9P 169454-01-7P

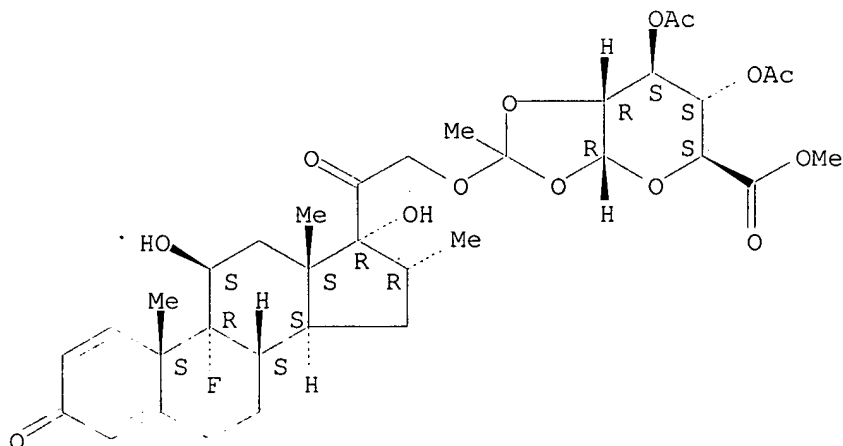
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate for prepn. of monosaccharide-substituted steroid compds. as **antiinflammatory** agents)

RN 169453-97-8 HCAPLUS

CN .alpha.-D-Glucopyranuronic acid, 1,2-O-[1-[[[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]oxy]ethylidene]-, methyl ester, 3,4-diacetate (9CI) (CA INDEX NAME)

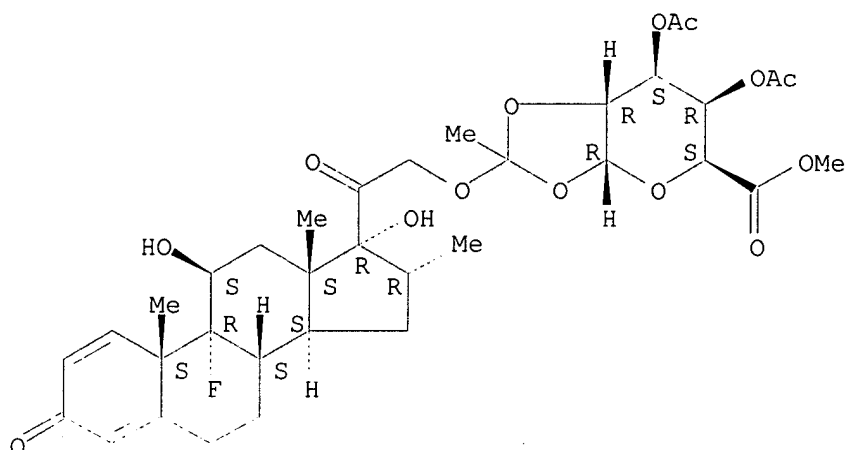
Absolute stereochemistry.



RN 169453-98-9 HCAPLUS

CN .alpha.-D-Galactopyranuronic acid, 1,2-O-[1-[[[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]oxy]ethylidene]-, methyl ester, 3,4-diacetate (9CI) (CA INDEX NAME)

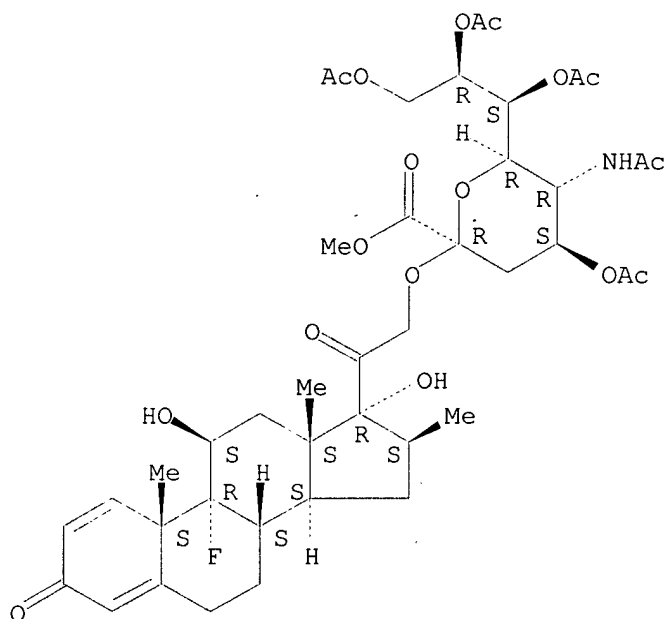
Absolute stereochemistry.



RN 169454-01-7 HCAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.beta.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, methyl ester, 4,7,8,9-tetraacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 4157-53-3P 6804-44-0P 88158-43-4P
 88158-45-6P 92901-23-0P 92901-30-9P
 152154-28-4P 153247-83-7P 153247-84-8P
 153247-87-1P 169453-45-6P 169453-46-7P
 169453-47-8P 169453-48-9P 169453-49-0P
 169453-50-3P 169453-51-4P 169453-52-5P
 169453-53-6P 169453-54-7P 169453-55-8P
 169453-56-9P 169453-57-0P 169453-58-1P
 169453-59-2P 169453-60-5P 169453-63-8P
 169453-64-9P 169453-65-0P 169453-66-1P
 169453-67-2P 169453-68-3P 169453-69-4P
 169453-70-7P 169453-71-8P 169453-72-9P
 169453-73-0P 169453-74-1P 169453-75-2P

169453-76-3P 169453-77-4P 169453-78-5P
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 169453-91-2P 169454-03-9P

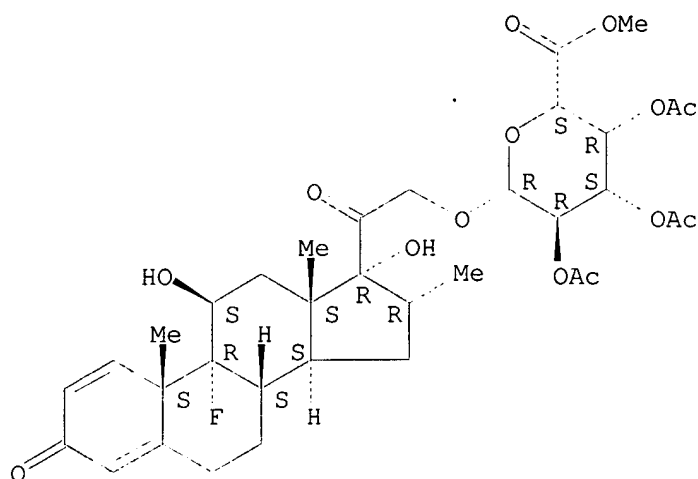
RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(prepn. of monosaccharide-substituted steroid compds. as
 antiinflammatory agents)

RN 4157-53-3 HCAPLUS

CN .beta.-D-Galactopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-
 dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester,
 2,3,4-triacetate (9CI) (CA INDEX NAME)

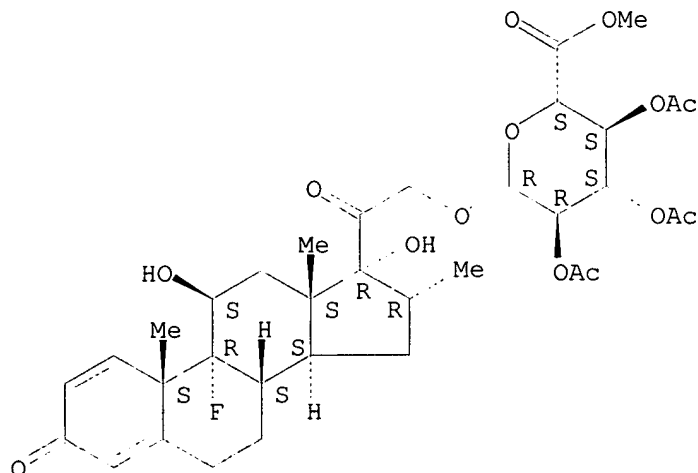
Absolute stereochemistry.



RN 6804-44-0 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-
 dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester,
 2,3,4-triacetate (9CI) (CA INDEX NAME)

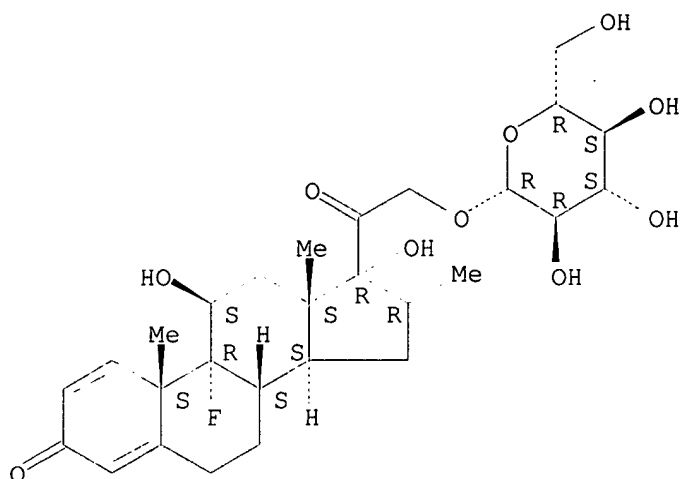
Absolute stereochemistry.



RN 88158-43-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

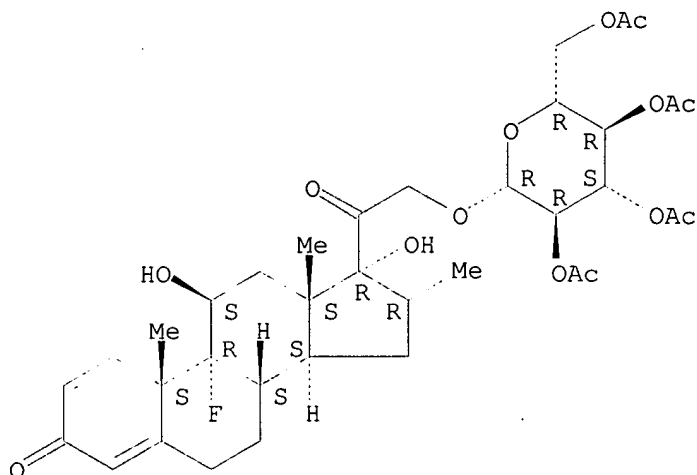
Absolute stereochemistry.



RN 88158-45-6 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

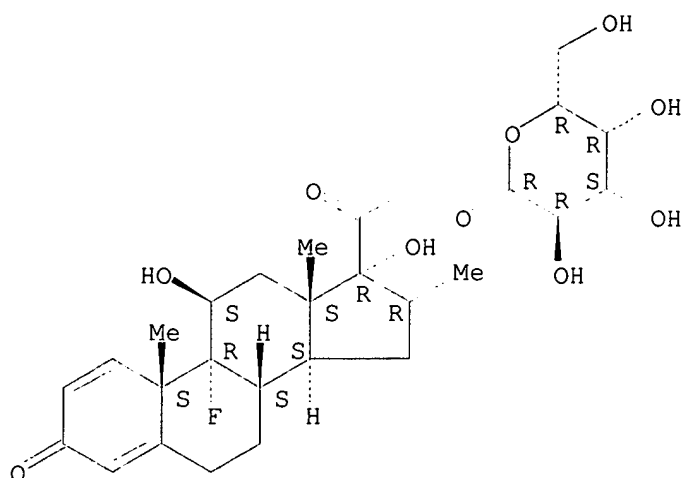
Absolute stereochemistry.



RN 92901-23-0 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

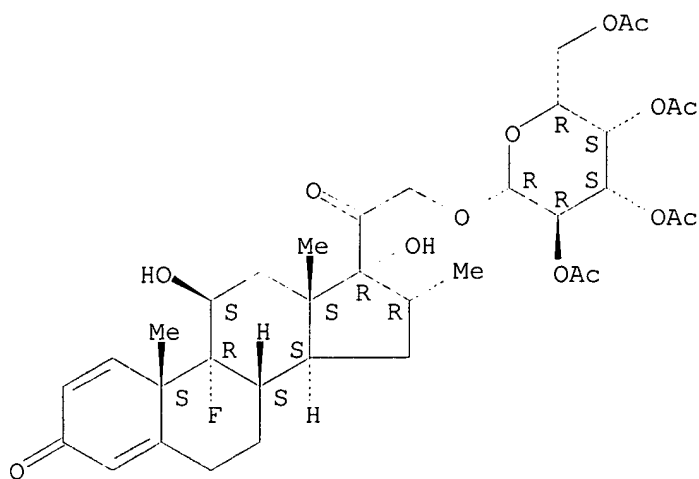
Absolute stereochemistry.



RN 92901-30-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-,
(11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

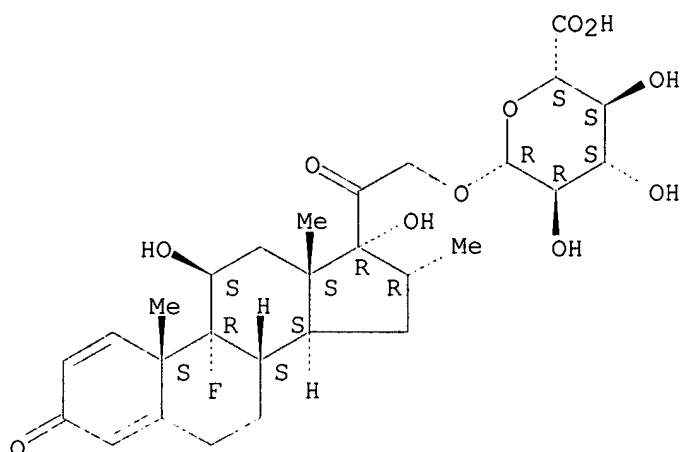
Absolute stereochemistry.



RN 152154-28-4 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-
dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

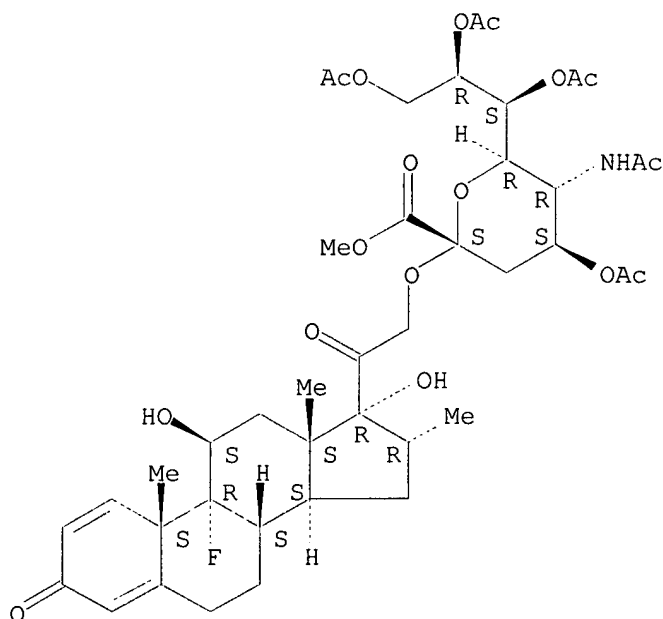
Absolute stereochemistry.



RN 153247-83-7 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, methyl ester, 4,7,8,9-tetraacetate (9CI) (CA INDEX NAME)

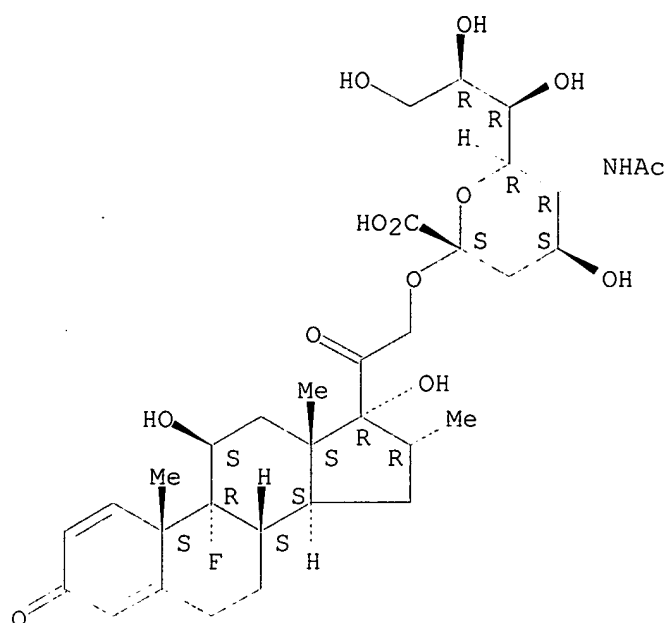
Absolute stereochemistry.



RN 153247-84-8 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]- (9CI) (CA INDEX NAME)

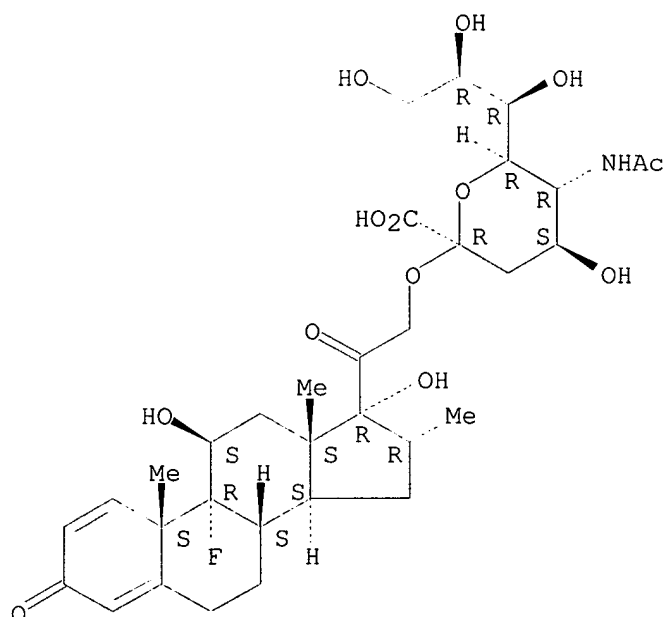
Absolute stereochemistry.



RN 153247-87-1 HCAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

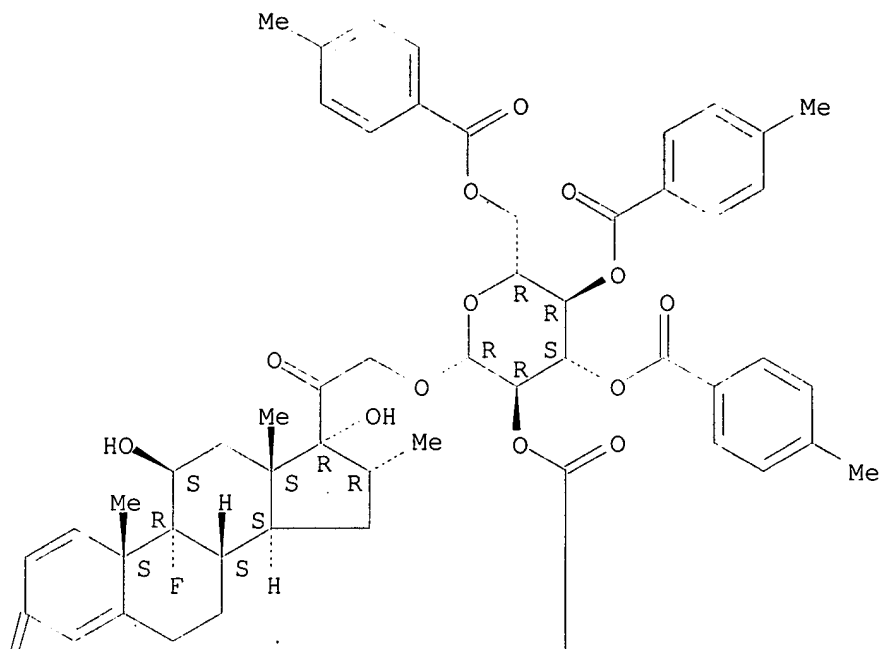


RN 169453-45-6 HCAPLUS

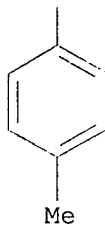
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.beta.-D-glucopyranosyl]oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

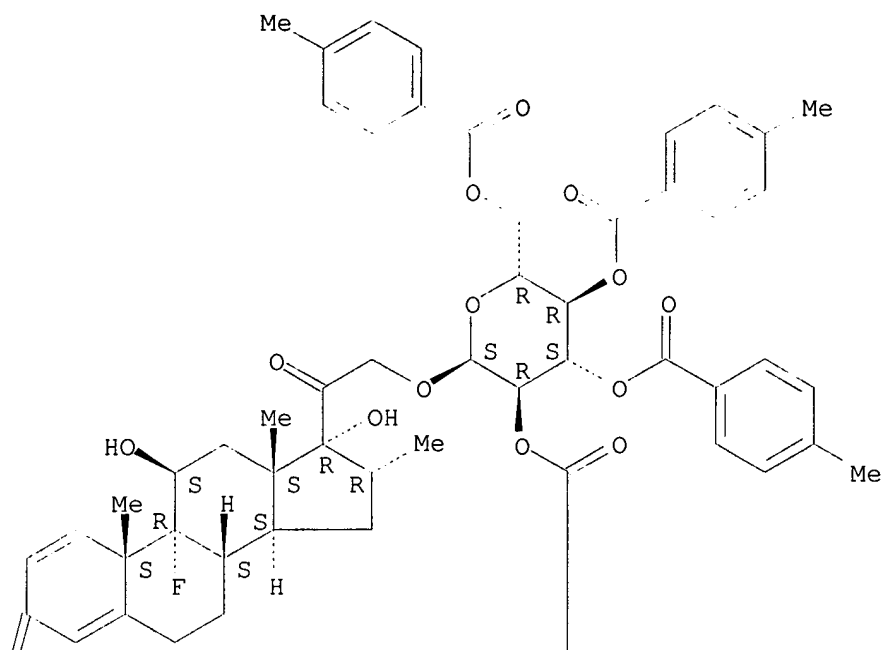


RN 169453-46-7 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
[[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.alpha.-D-glucopyranosyl]oxy]-,
(11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

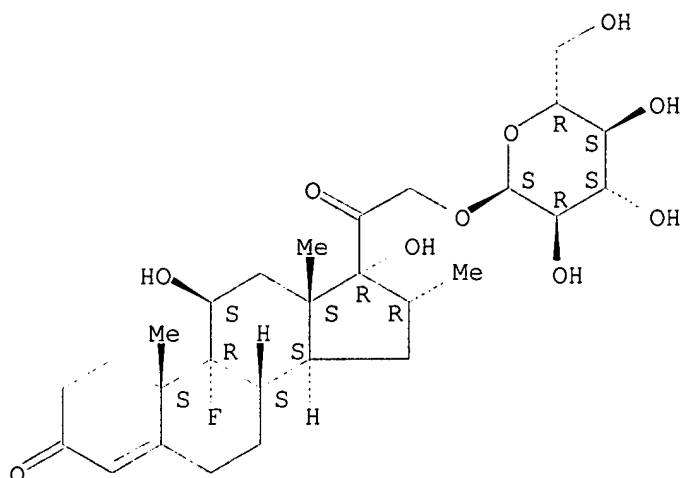


PAGE 2-A



RN 169453-47-8 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.alpha.-D-glucopyranosyloxy)-
 11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

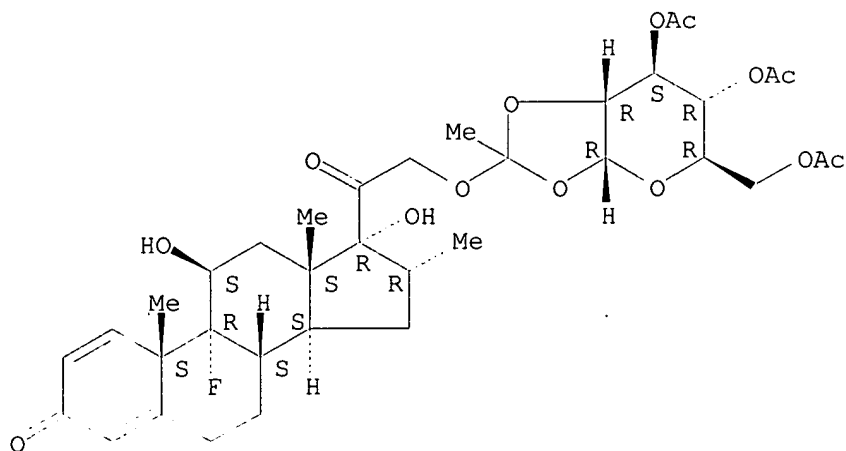
Absolute stereochemistry.



RN 169453-48-9 HCAPLUS

CN .alpha.-D-Glucopyranose, 1,2-O-[1-[[[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]oxy]ethylidene]-, 3,4,6-triacetate (9CI) (CA INDEX NAME)

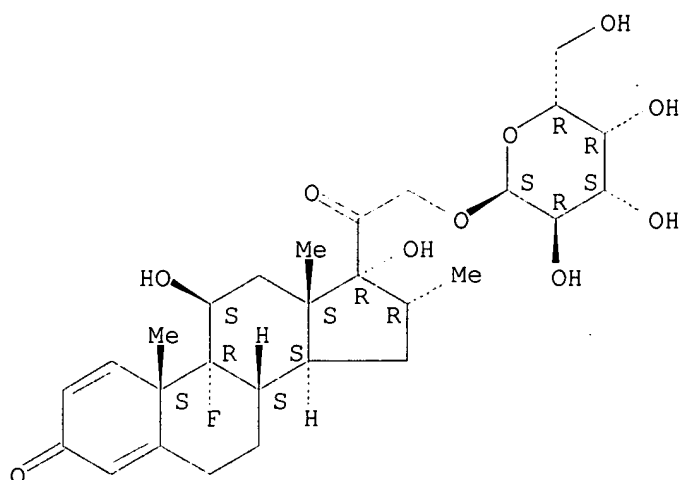
Absolute stereochemistry.



RN 169453-49-0 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[[[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.beta.-D-galactopyranosyl]oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

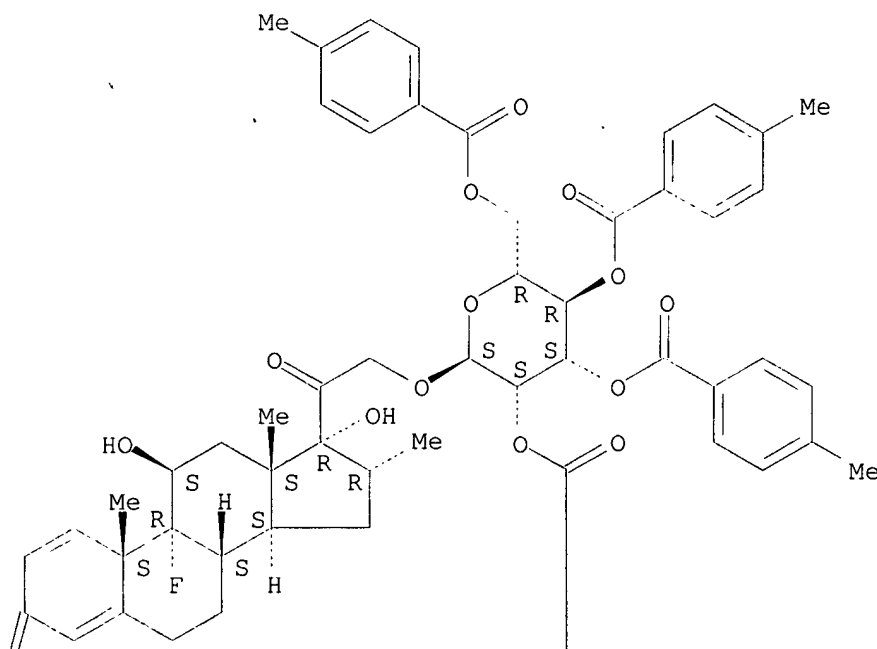


RN 169453-52-5 HCAPLUS

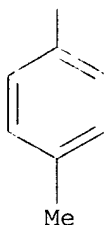
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
[[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.alpha.-D-mannopyranosyl]oxy]-,
(11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

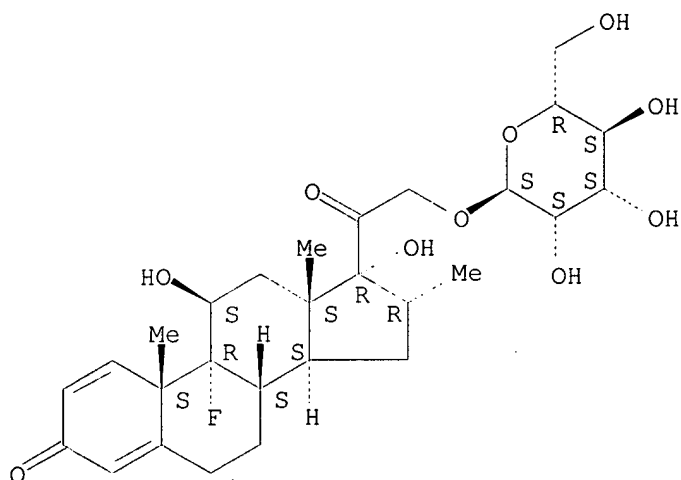


PAGE 2-A



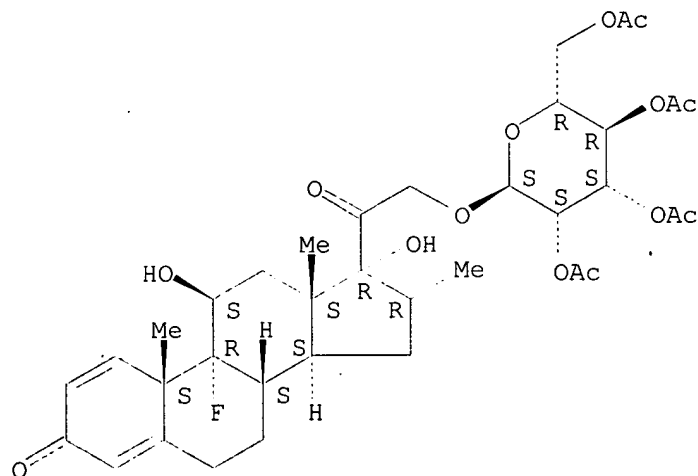
RN 169453-53-6 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.alpha.-D-mannopyranosyloxy)-
 11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169453-54-7 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [(2,3,4,6-tetra-O-acetyl-.alpha.-D-mannopyranosyl)oxy]-,
 (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

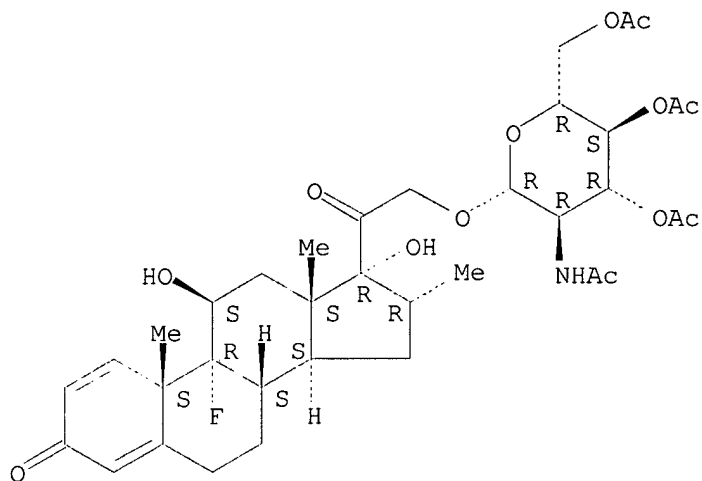
Absolute stereochemistry.



RN 169453-55-8 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[[3,4,6-tri-O-acetyl-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

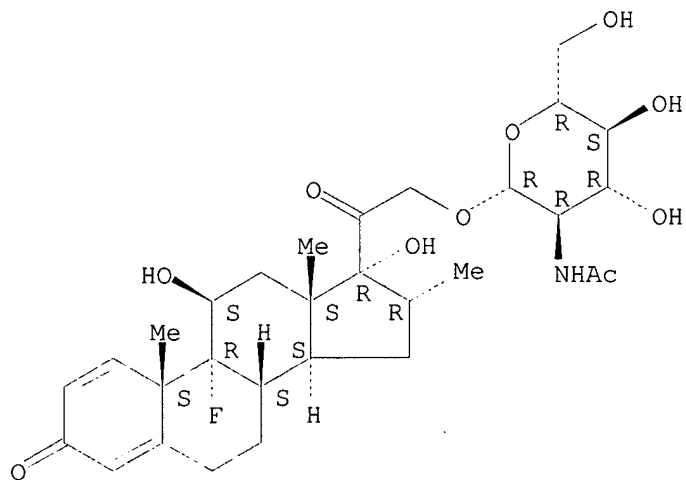
Absolute stereochemistry.



RN 169453-56-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]oxy]-9-fluoro-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

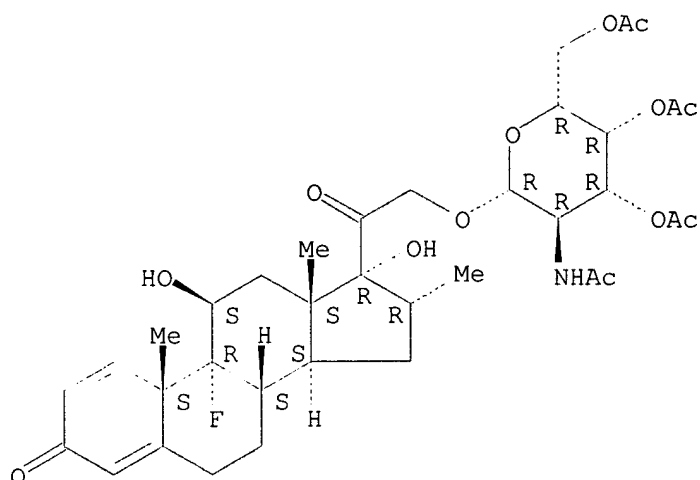
Absolute stereochemistry.



RN 169453-57-0 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[[3,4,6-tri-O-acetyl-2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl]oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

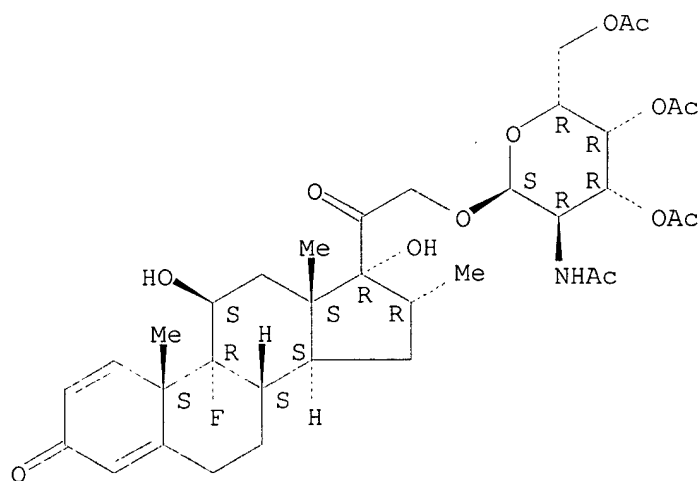
Absolute stereochemistry.



RN 169453-58-1 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[[3,4,6-tri-O-acetyl-2-(acetylamino)-2-deoxy-.alpha.-D-galactopyranosyl]oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

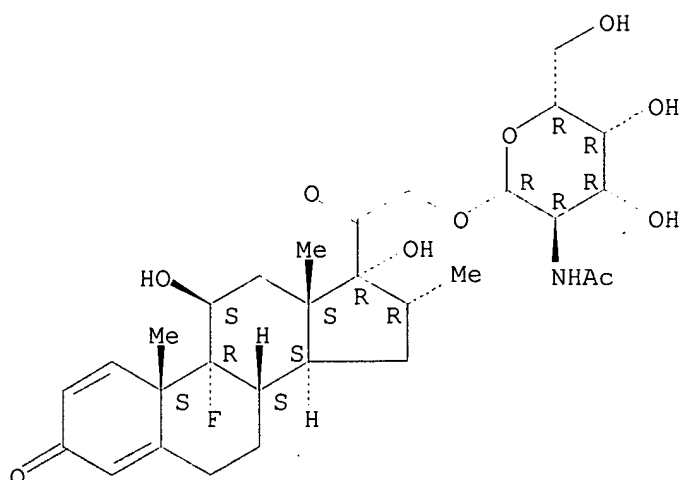
Absolute stereochemistry.



RN 169453-59-2 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[[2-(acetylamino)-2-deoxy-.beta.-D-galactopyranosyl]oxy]-9-fluoro-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

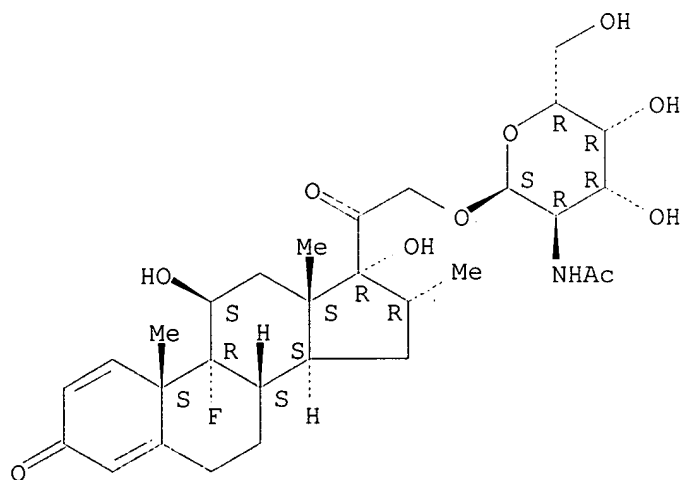
Absolute stereochemistry.



RN 169453-60-5 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[[2-(acetylamino)-2-deoxy-.alpha.-D-galactopyranosyl]oxy]-9-fluoro-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

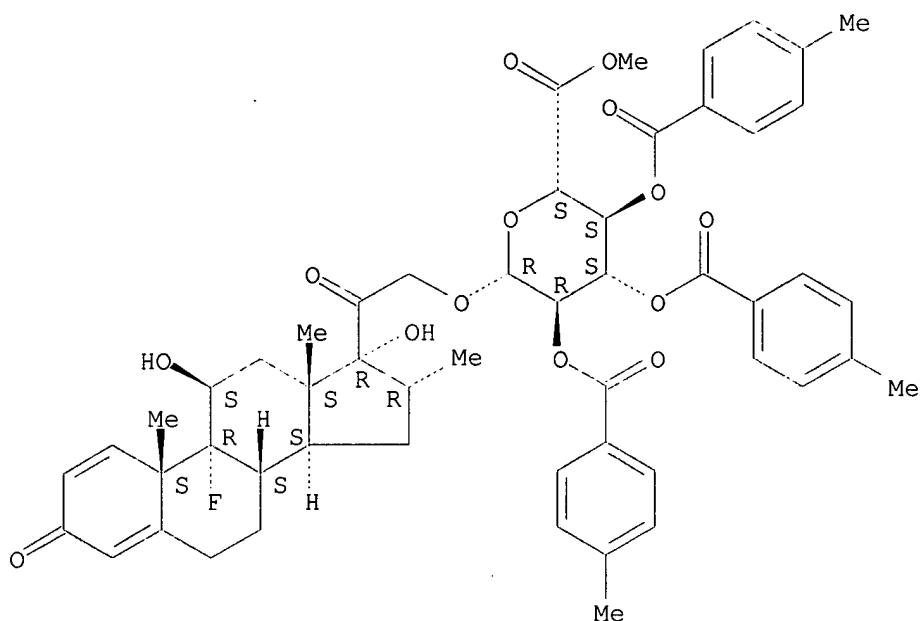
Absolute stereochemistry.



RN 169453-63-8 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-tris(4-methylbenzoate) (9CI) (CA INDEX NAME)

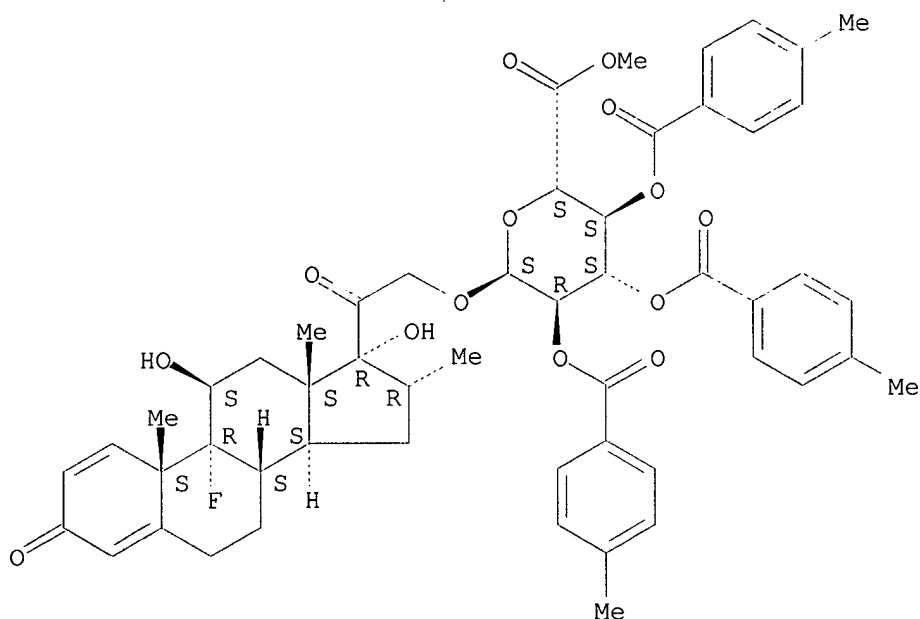
Absolute stereochemistry.



RN 169453-64-9 HCAPLUS

CN .alpha.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-tris(4-methylbenzoate) (9CI) (CA INDEX NAME)

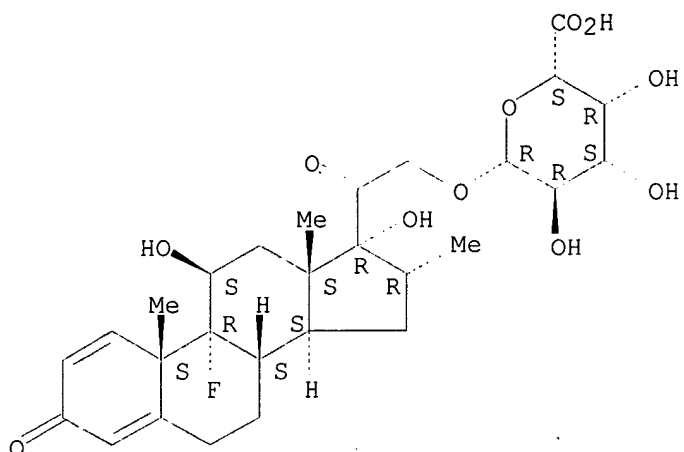
Absolute stereochemistry.



RN 169453-65-0 HCAPLUS

CN .beta.-D-Galactopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

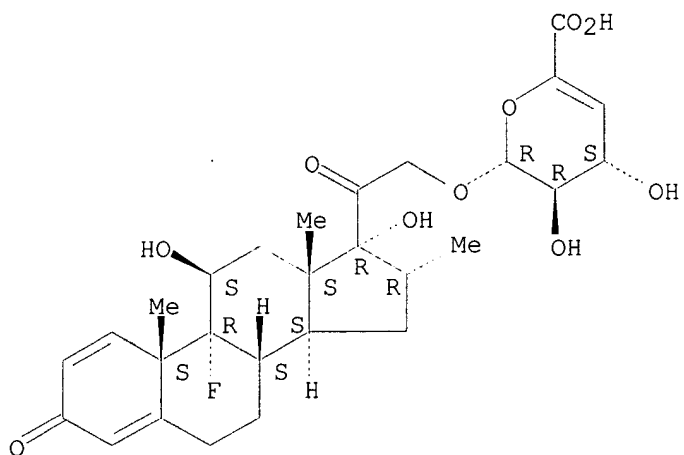
Absolute stereochemistry.



RN 169453-66-1 HCAPLUS

CN .alpha.-L-threo-Hex-4-enopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl 4-deoxy-(9CI) (CA INDEX NAME)

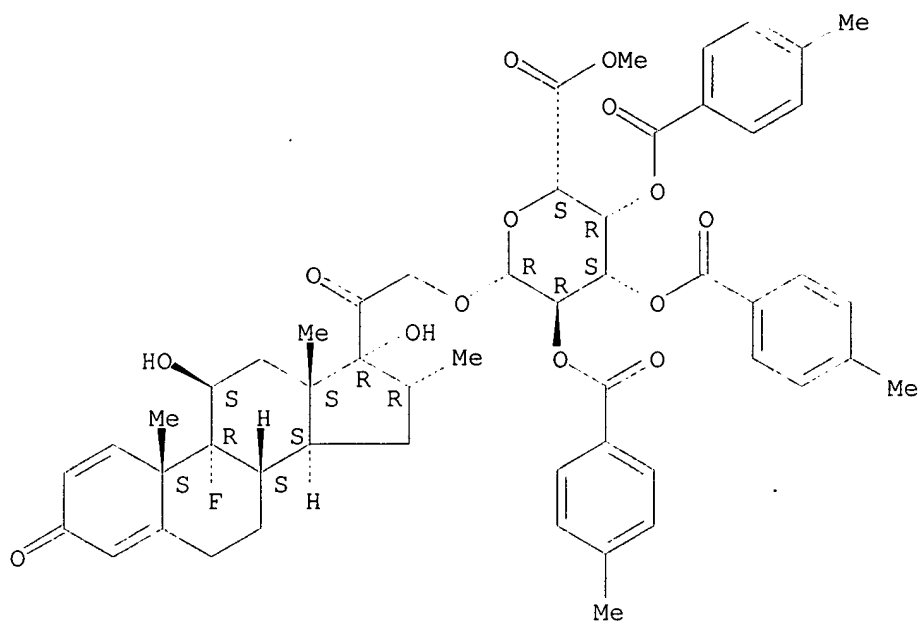
Absolute stereochemistry.



RN 169453-67-2 HCAPLUS

CN .beta.-D-Galactopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-tris(4-methylbenzoate) (9CI) (CA INDEX NAME)

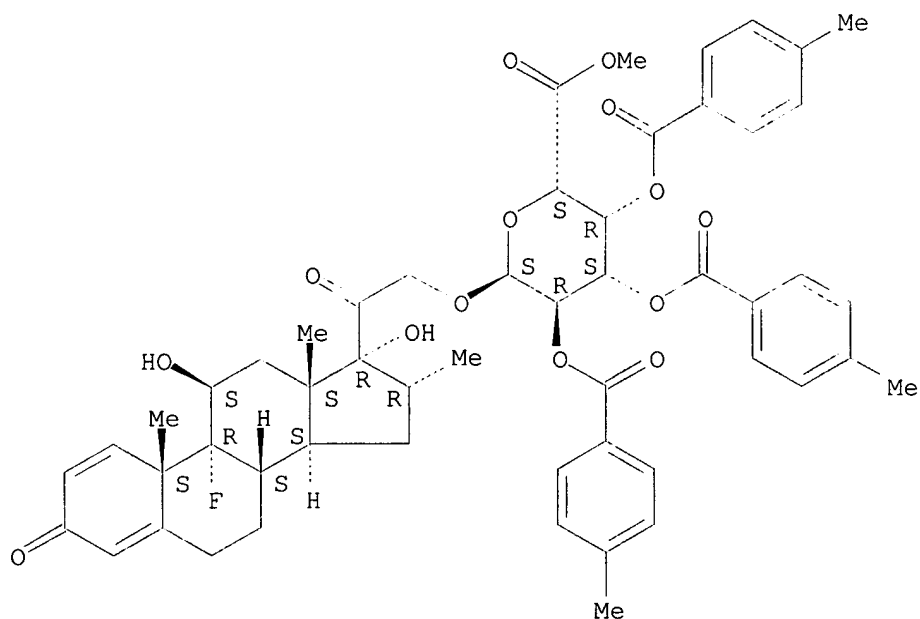
Absolute stereochemistry.



RN 169453-68-3 HCAPLUS

CN .alpha.-D-Galactopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-tris(4-methylbenzoate) (9CI) (CA INDEX NAME)

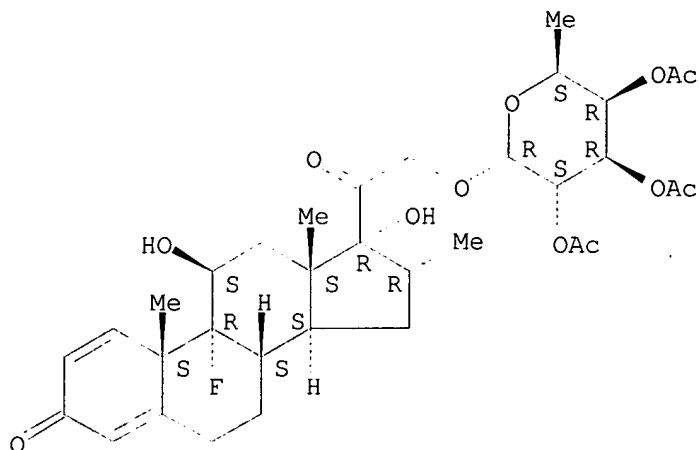
Absolute stereochemistry.



RN 169453-69-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4-tri-O-acetyl-6-deoxy-.alpha.-L-galactopyranosyl)oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

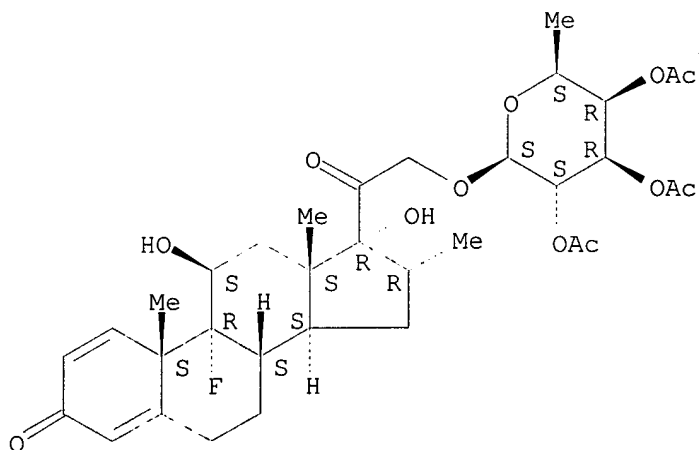
Absolute stereochemistry.



RN 169453-70-7 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4-tri-O-acetyl-6-deoxy-.beta.-L-galactopyranosyl)oxy]-, (11.beta.,16.alpha.)-(9CI) (CA INDEX NAME)

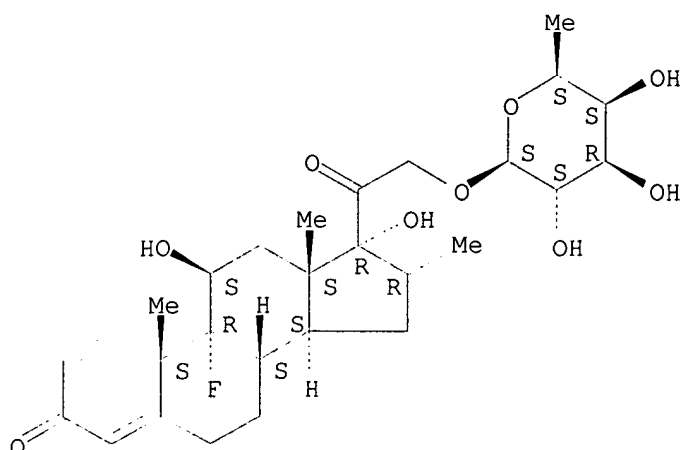
Absolute stereochemistry.



RN 169453-71-8 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[(6-deoxy-.beta.-L-galactopyranosyl)oxy]-9-fluoro-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)-(9CI) (CA INDEX NAME)

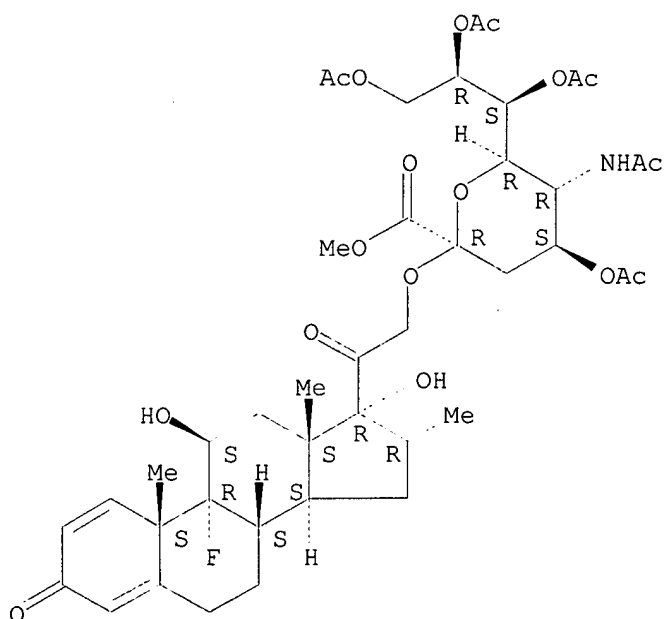
Absolute stereochemistry.



RN 169453-72-9 HCAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, methyl ester, 4,7,8,9-tetraacetate (9CI) (CA INDEX NAME)

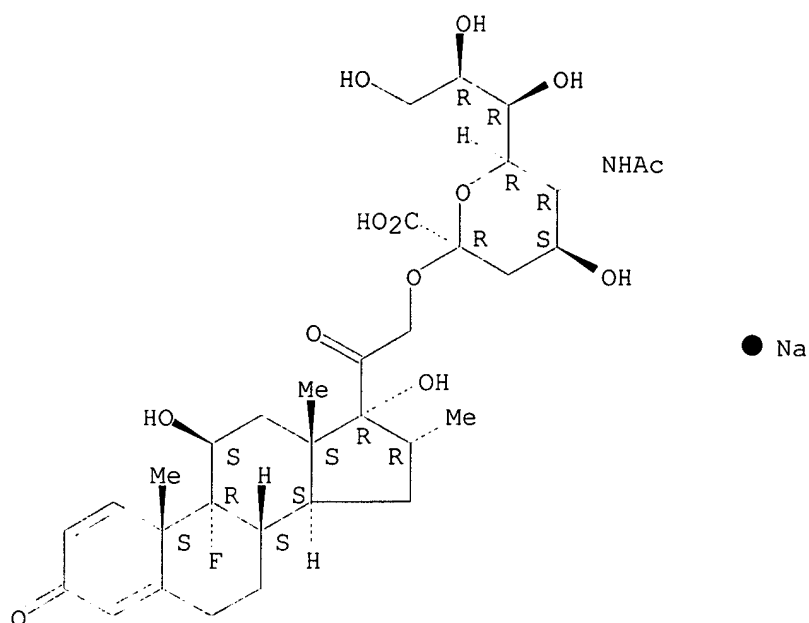
Absolute stereochemistry.



RN 169453-73-0 HCAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, monosodium salt (9CI) (CA INDEX NAME)

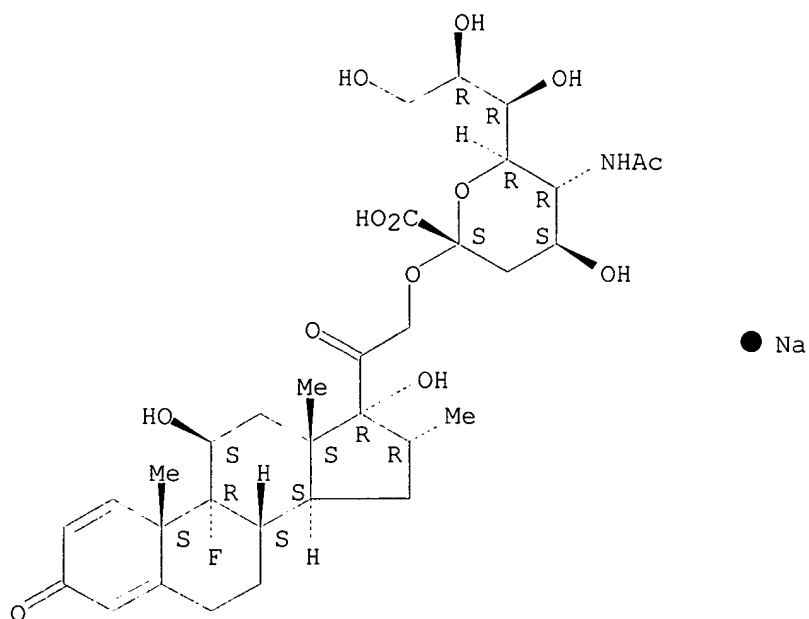
Absolute stereochemistry.



RN 169453-74-1 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, monosodium salt
(9CI) (CA INDEX NAME)

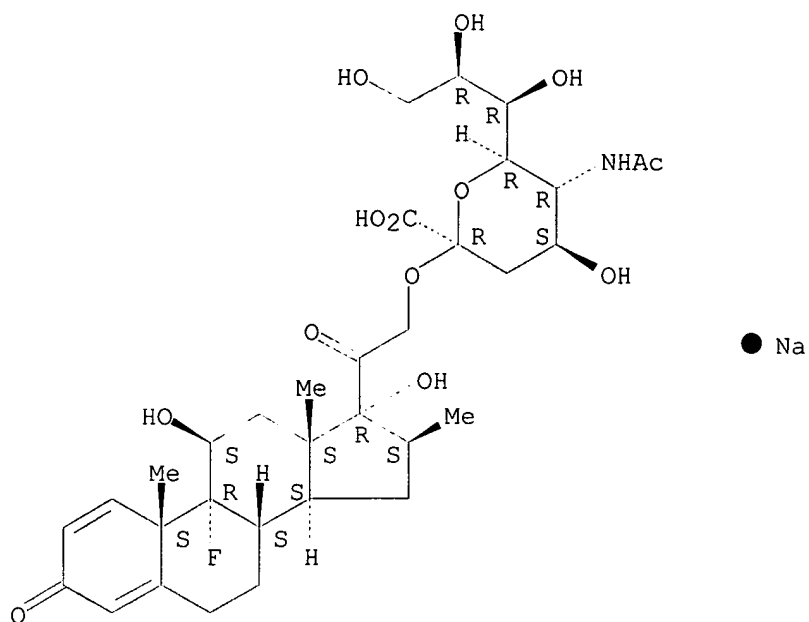
Absolute stereochemistry.



RN 169453-75-2 HCAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.beta.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, monosodium salt
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

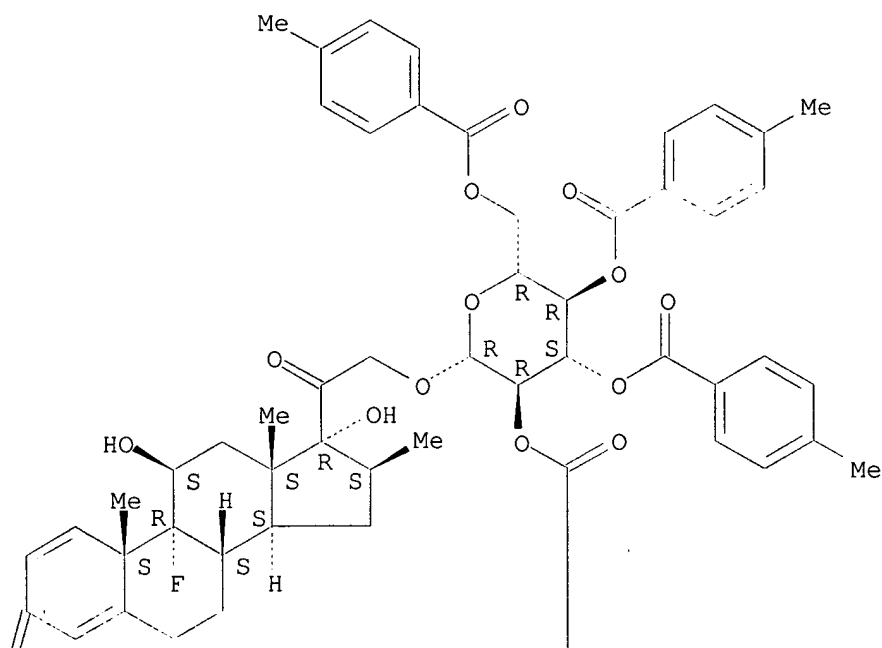


RN 169453-76-3 HCAPLUS

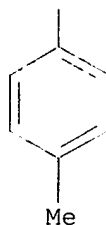
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
[[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.beta.-D-glucopyranosyl]oxy]-,
(11.beta.,16.beta.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



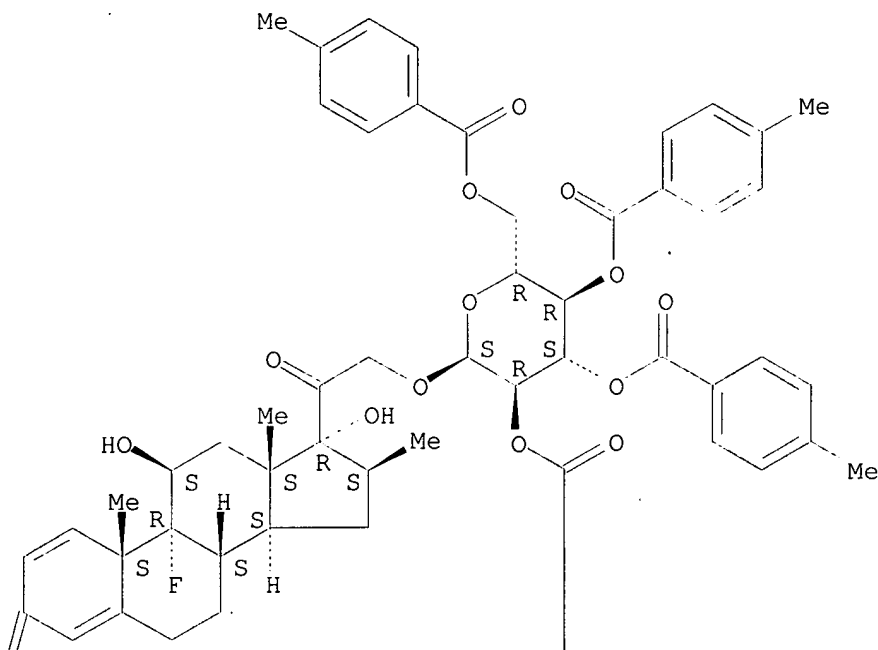
PAGE 2-A



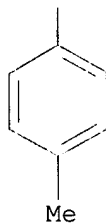
RN 169453-77-4 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.alpha.-D-glucopyranosyl]oxy]-,
 (11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



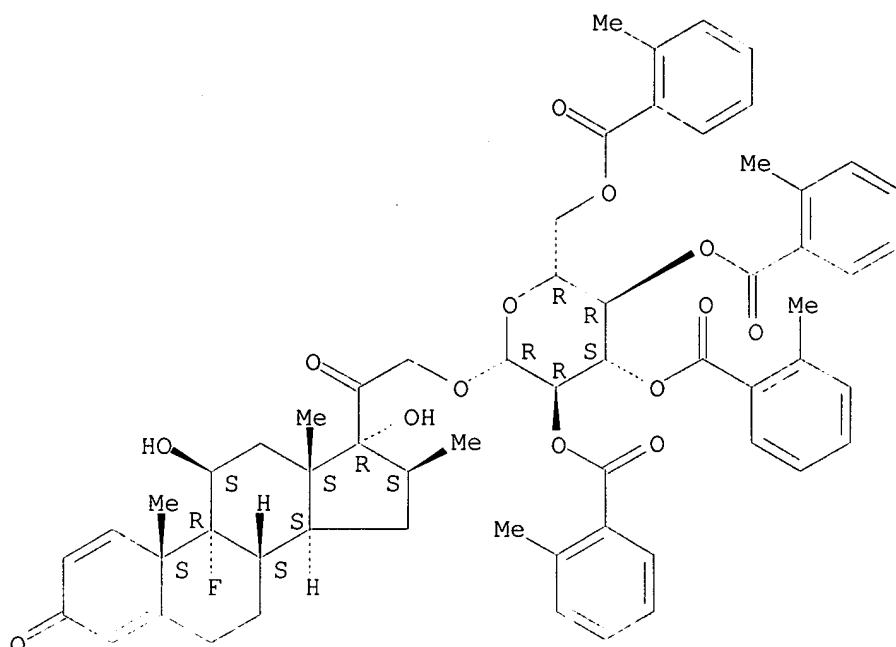
PAGE 2-A



RN 169453-78-5 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [[2,3,4,6-tetrakis-O-(2-methylbenzoyl)-.beta.-D-glucopyranosyl]oxy]-,

(11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

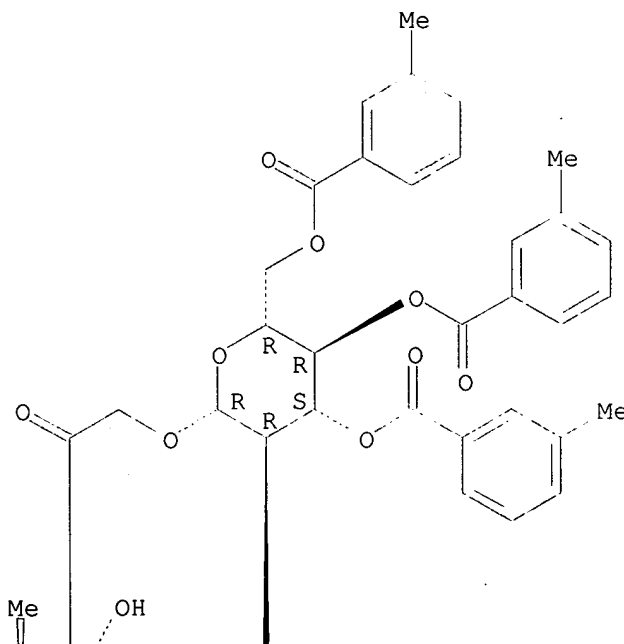


RN 169453-79-6 HCAPLUS

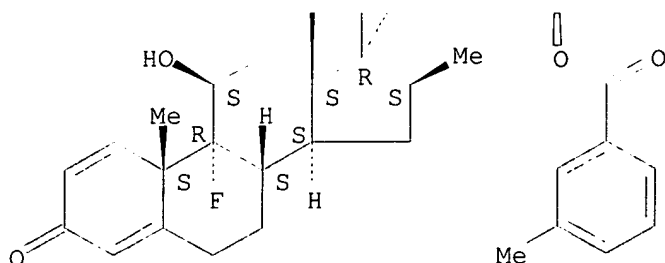
CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
[[2,3,4,6-tetrakis-O-(3-methylbenzoyl)-.beta.-D-glucopyranosyl]oxy]-,
(11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



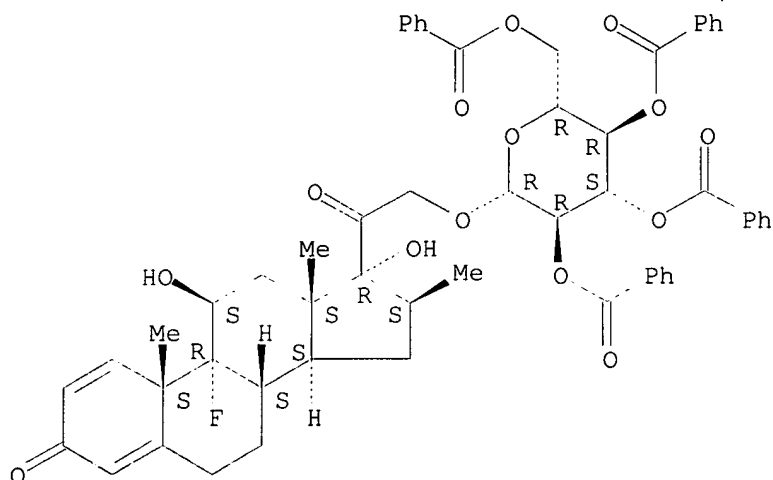
PAGE 2-A



RN 169453-80-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [(2,3,4,6-tetra-O-benzoyl-.beta.-D-glucopyranosyl)oxy]-,
 (11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

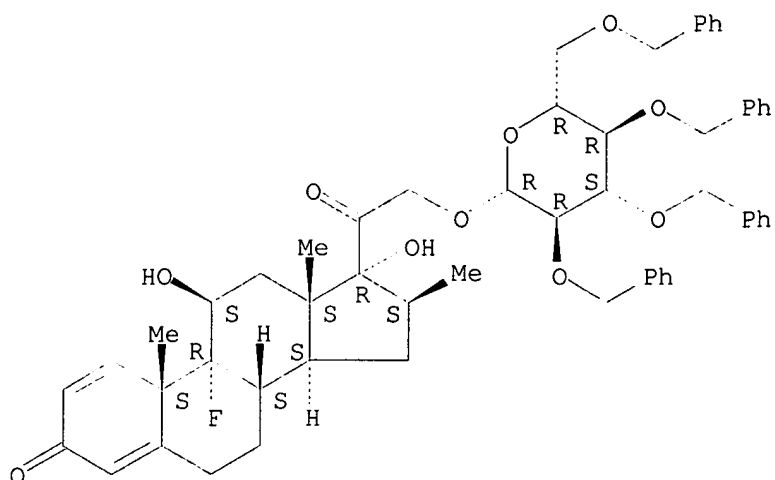
Absolute stereochemistry.



RN 169453-81-0 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [[2,3,4,6-tetrakis-O-(phenylmethyl)-.beta.-D-glucopyranosyl]oxy]-,
 (11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

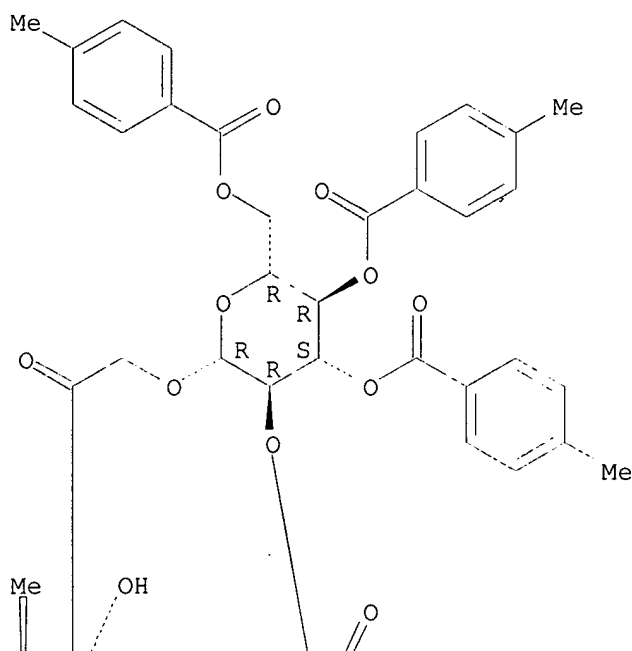


RN 169453-82-1 HCAPLUS

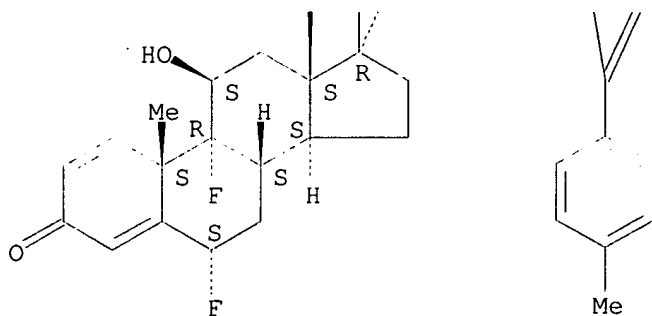
CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,17-dihydroxy-21-[[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.beta.-D-glucopyranosyl]oxy]-, (6.alpha.,11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



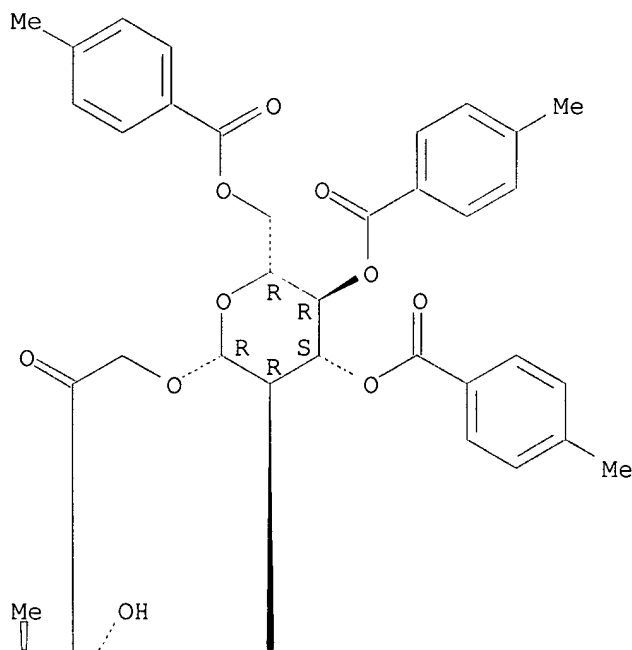
PAGE 2-A



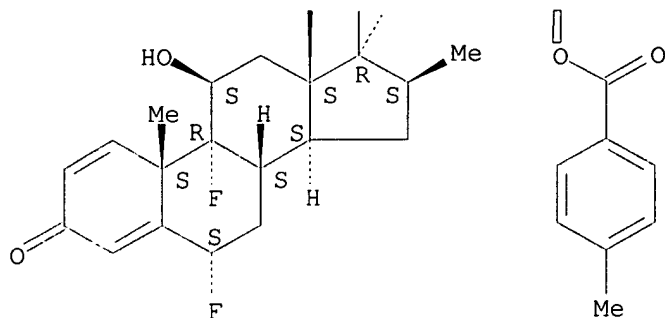
RN 169453-83-2 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,17-dihydroxy-16-methyl-21-
 [[2,3,4,6-tetrakis-O-(4-methylbenzoyl)-.beta.-D-glucopyranosyl]oxy]-,
 (6.alpha.,11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



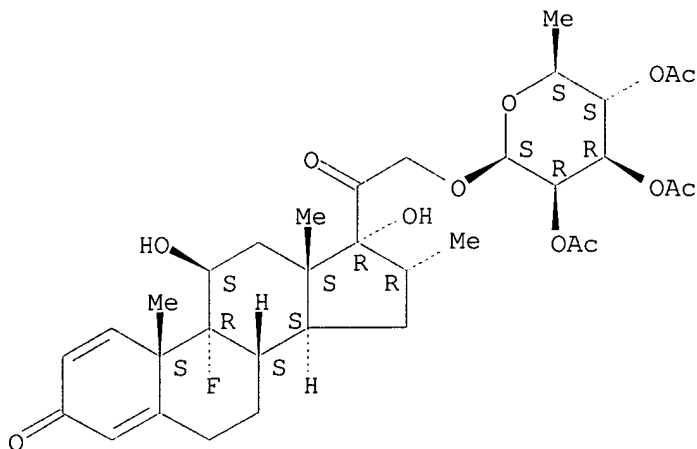
PAGE 2-A



RN 169453-90-1 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4-tri-O-acetyl-6-deoxy-.beta.-L-mannopyranosyl)oxy]-, (11.beta.,16.alpha.)-(9CI) (CA INDEX NAME)

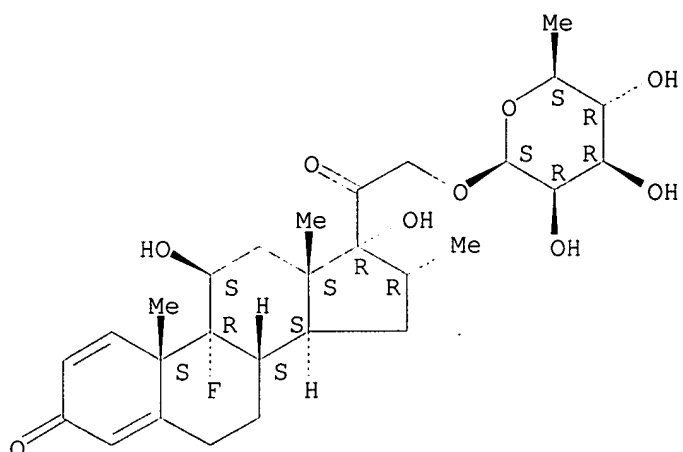
Absolute stereochemistry.



RN 169453-91-2 HCAPLUS

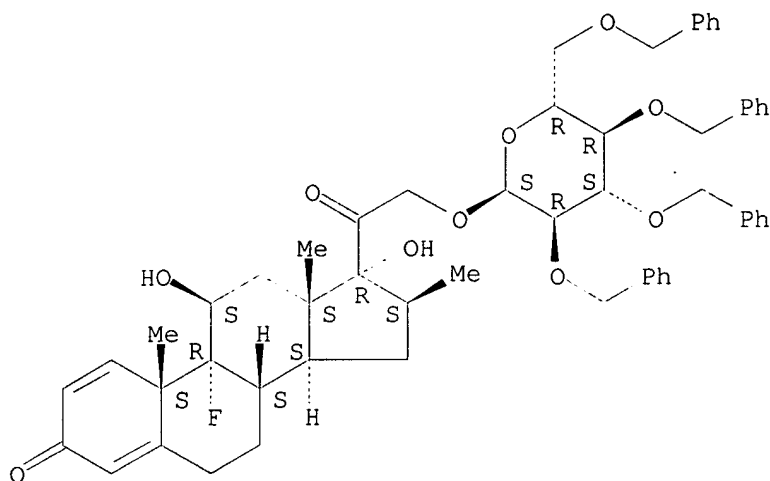
CN Pregna-1,4-diene-3,20-dione, 21-[(6-deoxy-.beta.-L-mannopyranosyl)oxy]-9-fluoro-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169454-03-9 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [[2,3,4,6-tetrakis-O-(phenylmethyl)-.alpha.-D-glucopyranosyl]oxy]-,
 (11.beta.,16.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

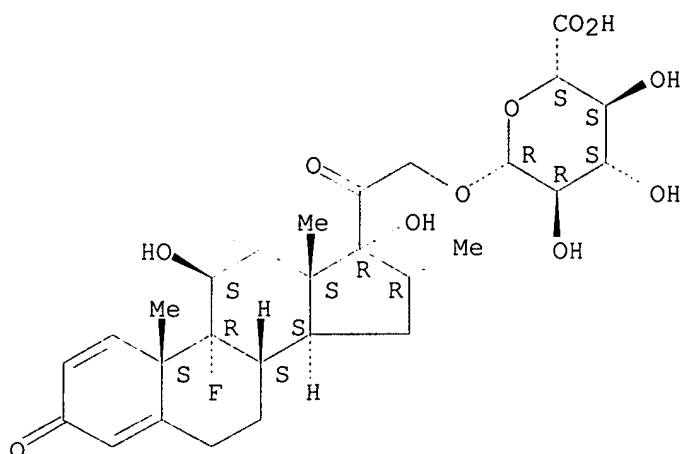


L103 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1995:762890 HCAPLUS
 DN 123:161106
 TI A novel colon-specific steroid prodrug enhances sodium chloride absorption
 in rat colitis
 AU Fedorak, Richard N.; Cui, Ningren; Friend, David R.; Madsen, Karen L.;
 Empey, Lonnie R.
 CS Dep. Medicine, Univ. Alberta, Edmonton, AB, T6G 2C2, Can.
 SO American Journal of Physiology (1995), 269(2, Pt. 1), G210-G218
 CODEN: AJPHAP; ISSN: 0002-9513
 PB American Physiological Society
 DT Journal
 LA English
 CC 2-4 (Mammalian Hormones)
 AB A recently synthesized novel colon-specific dexamethasone prodrug,
 dexamethasone-.beta.-D-glucuronide, delivers efficacious amts. of
 dexamethasone to the colon with limited adrenal suppressive effects.

During exptl. induced colitis in rats, the dexamethasone prodrug is significantly more potent than free dexamethasone in improving colonic fluid and electrolyte absorptive injury. The present studies examd. whether the improvement in colonic absorption seen with the prodrug occurred as a consequence of alterations in sodium and chloride epithelial transport. The efficacy of the dexamethasone prodrug and free dexamethasone were tested in an acetic acid-induced rat model of colitis. Healing of the induced colitis was assessed by measuring net colonic fluid absorption and surface area ulceration. Transmural unidirectional fluxes of ^{22}Na and ^{36}Cl across sheets of colonic mucosa were measured in Ussing chambers. Treatment of colitis with the prodrug delivered a 6-fold higher concn. of dexamethasone to the colon than did treatment with the free drug. The prodrug accelerated healing of colitis by returning in vivo colonic fluid absorption to normal and virtually eliminated colonic macroscopic ulceration, whereas the free drug did not. In vitro transmural fluxes demonstrated that, in addn. to repair of mucosal integrity, the prodrug enhanced electroneutral NaCl absorption over and above that seen in control animals or after treatment with the free drug. Both the prodrug and the free drug limited theophylline-mediated net Cl^- and Na^+ secretion, an effect that would be consistent with the antidiarrheal effect induced by these drugs in vivo. Apparently, treatment of exptl. induced colitis with the novel colon-specific prodrug, dexamethasone-.beta.-D-glucuronide, has distinct mucosal healing and antidiarrheal advantages over administration of its parent, free dexamethasone. Specifically, dexamethasone prodrug treatment enhances NaCl absorptive effects and limits cAMP-mediated secretion of colonic epithelia.

- ST dexamethasone glucuronide colitis salt absorption
 IT Intestine, disease
 (colitis, colon-specific dexamethasone glucuronide enhances NaCl absorption in rat colitis)
 IT 50-02-2, Dexamethasone 152154-28-4, Dexamethasone-.beta.-D-glucuronide
 RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (colon-specific dexamethasone glucuronide enhances NaCl absorption in rat colitis)
 IT 7647-14-5, Sodium chloride (NaCl), biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (colon-specific dexamethasone glucuronide enhances NaCl absorption in rat colitis)
 IT 152154-28-4, Dexamethasone-.beta.-D-glucuronide
 RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (colon-specific dexamethasone glucuronide enhances NaCl absorption in rat colitis)
 RN 152154-28-4 HCAPLUS
 CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:646178 HCAPLUS

DN 123:48079

TI Colonic delivery of dexamethasone from a prodrug accelerates healing of colitis in rats without adrenal suppression

AU Fedorak, Richard N.; Haeberlin, Barbara; Empey, Lonnie R.; Cui, Ningren; Nolen, Harold; Jewell, Laurence D.; Friend, David R.

CS Controlled Release and Biomedical Polymers Department, SRI International, Menlo Park, CA, USA

SO Gastroenterology (1995), 108(6), 1688-99

CODEN: GASTAB; ISSN: 0016-5085

DT Journal

LA English

CC 2-4 (Mammalian Hormones)

AB Dexamethasone-.beta.-D-glucuronide, a colon-specific prodrug of dexamethasone, may be useful in the treatment of ulcerative colitis and Crohn's colitis. The aim of this study was to evaluate colonic delivery and efficacy of this prodrug in the rat. Distribution of dexamethasone in luminal contents and tissues of the gastrointestinal tract and in plasma was measured after oral administration of dexamethasone-.beta.-D-glucuronide or free dexamethasone. Efficacy of the prodrug and free drug was tested in an acetic acid-induced rat colitis model. Healing of induced colitis was assessed by measuring net intestinal fluid absorption, colonic surface area of ulceration, histol., and myeloperoxidase activity. Glucocorticosteroid toxicity was evaluated with serum corticosterone and plasma adrenocorticotrophic hormone levels. The drug delivery index (a measure of relative targeting efficiency) was 6.7 and 8.6 in the cecal and colonic mucosa, resp. The prodrug was significantly more potent than free drug in improving net colonic fluid absorption while significantly reducing surface area of ulceration and histol. grade in colitic rats. Treatment with free dexamethasone significantly reduced serum corticosterone levels to subnormal levels, and treatment with the prodrug maintained serum corticosterone and plasma adrenocorticotrophic hormone levels near control levels. The prodrug dexamethasone-.beta.-D-glucuronide delivers efficacious amts. of dexamethasone to the large intestine from lower doses than free dexamethasone.

ST colon delivery dexamethasone prodrug colitis

IT Intestine, disease

(colitis, dexamethasone prodrug colonic delivery effect on)

IT 152154-28-4, Dexamethasone-.beta.-D-glucuronide

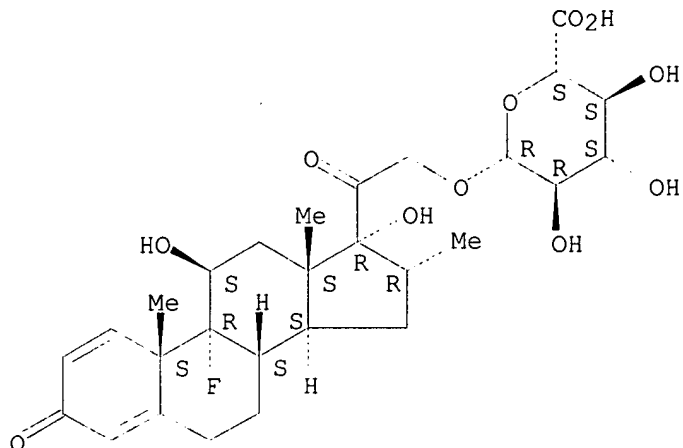
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(effect on colitis by colonic delivery without suppressing adrenal

cortex)
 IT 152154-28-4, Dexamethasone-.beta.-D-glucuronide
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (effect on colitis by colonic delivery without suppressing adrenal
 cortex)
 RN 152154-28-4 HCAPLUS
 CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-
 dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

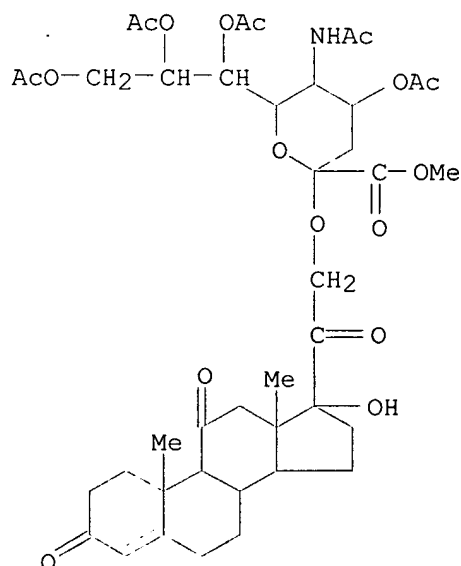
Absolute stereochemistry.



L103 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1994:135071 HCAPLUS
 DN 120:135071
 TI Preparation of novel longer-acting sialylsteroids
 IN Numata, Masaaki; Ishii, Takayuki; Sugimoto, Mamoru; Sugai, Kei; Sugiyama,
 Naokazu; Ogawa, Tomoya
 PA Mect Corp., Japan
 SO PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 IC ICM C07H015-203
 ICS C07J017-00
 CC 33-8 (Carbohydrates)
 Section cross-reference(s): 1, 32
 FAN.CNT 1

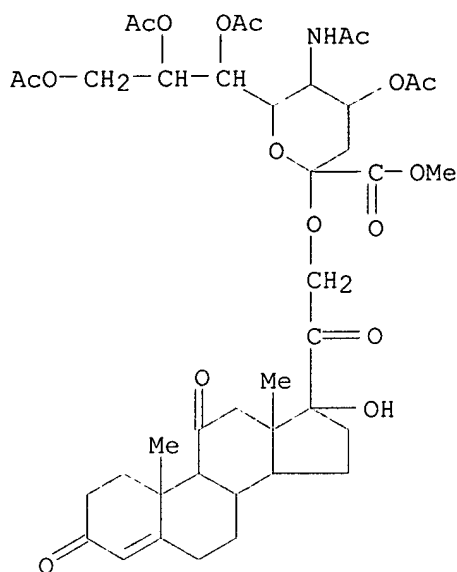
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | WO 9321198 | A1 | 19931028 | WO 1993-JP466 | 19930413 <-- |
| | W: AU, CA, FI, HU, KR, NO, RU, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | JP 05286992 | A2 | 19931102 | JP 1992-92953 | 19920413 <-- |
| | AU 9339042 | A1 | 19931118 | AU 1993-39042 | 19930413 <-- |
| PRAI | JP 1992-92953 | | 19920413 | <-- | |
| | WO 1993-JP466 | | 19930413 | <-- | |
| OS | MARPAT 120:135071 | | | | |
| GI | | | | | |

- AB Title compds. I and II [R1 = steroid residue such as Q, Q1, Q2; R2 = H, Ac; R3 = H, alkyl], having the usual steroidal effect but longer-acting than the existing analogs, are prepd. E.g., a mixt. of Q-OH and 2-chloro-4,7,8,9-tetra-O-acetyl-N-acetylneuraminic acid Me ester in CH₂Cl₂ contg. mol. sieves 4A, Hg(CN)₂, and HgBr₂ was stirred at -10.degree. for 40 h to give I and II [R1 = Q, R2 = Ac, R3 = Me]. In a study using guinea pigs the **antiinflammatory** activity of sialyldexamethasone (.alpha.-form) was ca. 1/10 that of dexamethasone phosphate in inhibiting the carrageenin-induced **inflammation**.
- ST sialylsteroid prepn **antiinflammatory antiallergy**;
steroid sialyl prepn
- IT Steroids, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(sialyl, prepn. of, as **antiinflammatory** and **antiallergic** agents)
- IT **Allergy inhibitors**
Inflammation inhibitors
(sialylsteroids)
- IT 153247-80-4P 153247-81-5P 153247-82-6P
153247-83-7P 153247-84-8P 153247-85-9P 153247-86-0P
153247-87-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antiinflammatory** and **antiallergic** agent)
- IT 50-02-2, Dexamethasone 53-06-5 67-97-0, Vitamin D3 132883-18-2,
2-Chloro-4,7,8,9-tetra-O-acetyl-N-acetylneuraminic acid methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant, in prepn. of sialylsteroids as **antiinflammatory** and **antiallergic** agents)
- IT 153247-80-4P 153247-81-5P 153247-82-6P
153247-83-7P 153247-84-8P 153247-87-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antiinflammatory** and **antiallergic** agent)
- RN 153247-80-4 HCAPLUS
- CN .alpha.-Neuraminic acid, N-acetyl-2-O-(17-hydroxy-3,11,20-trioxopregn-4-en-21-yl)-, methyl ester, 4,7,8,9-tetraacetate (9CI) (CA INDEX NAME)



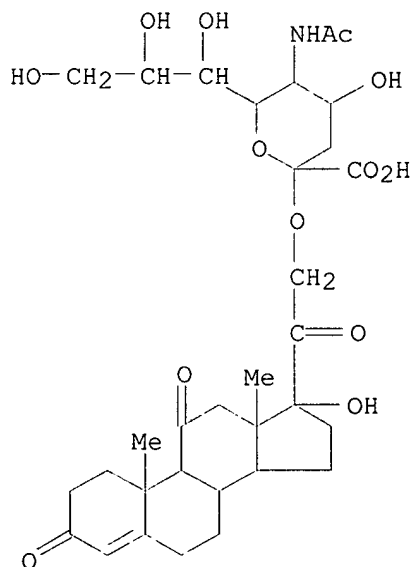
RN 153247-81-5 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-(17-hydroxy-3,11,20-trioxopregn-4-en-21-yl)-, methyl ester, 4,7,8,9-tetraacetate (9CI) (CA INDEX NAME)



RN 153247-82-6 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-(17-hydroxy-3,11,20-trioxopregn-4-en-21-yl)-, monosodium salt (9CI) (CA INDEX NAME)

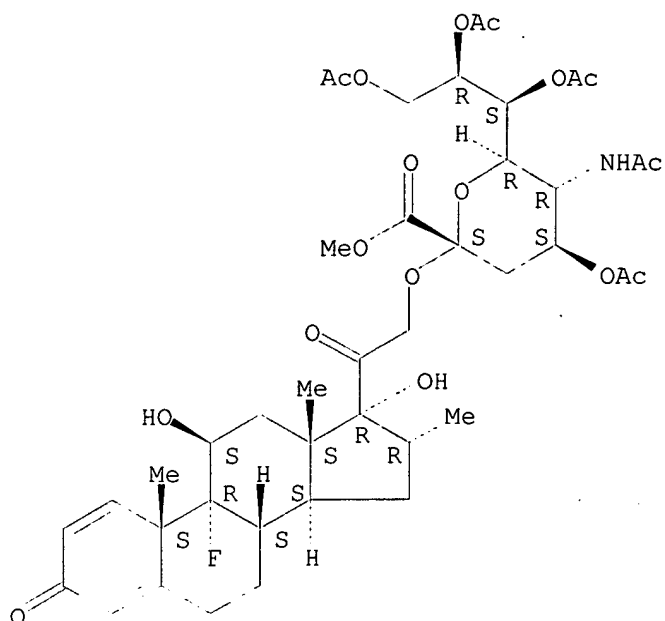


● Na

RN 153247-83-7 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]-, methyl ester, 4,7,8,9-tetraacetate (9CI) (CA INDEX NAME)

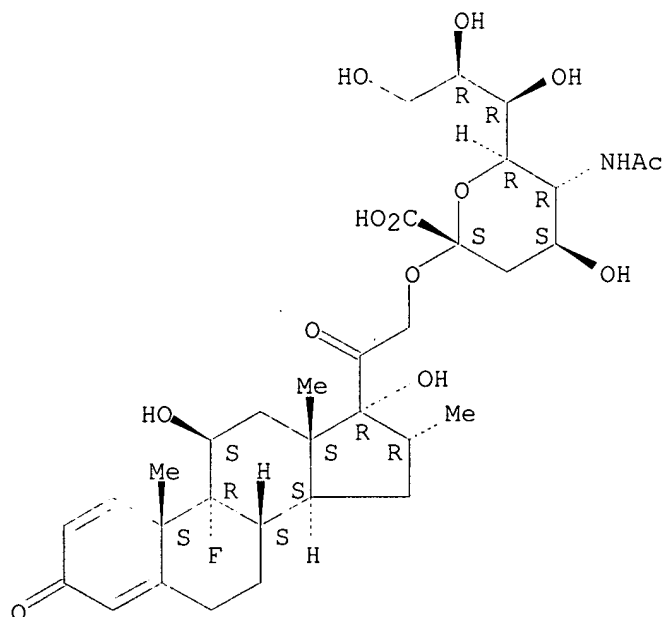
Absolute stereochemistry.



RN 153247-84-8 HCAPLUS

CN .beta.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]- (9CI) (CA INDEX NAME)

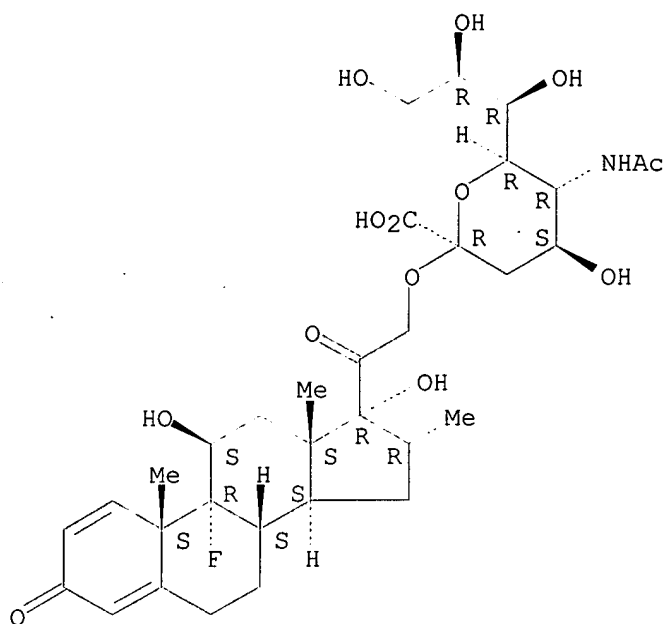
Absolute stereochemistry.



RN 153247-87-1 HCAPLUS

CN .alpha.-Neuraminic acid, N-acetyl-2-O-[(11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:38138 HCAPLUS

DN 120:38138

TI Pharmaceutical compositions and methods for colonic delivery of corticosteroids

IN Friend, David R.; Fedorak, Richard N.

PA SRI International, USA

SO PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07J017-00

ICS C07J071-00; A61K031-58; A61K031-70

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 32, 33

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|----------|
| PI | WO 9322334 | A1 | 19931111 | WO 1993-US4202 | 19930503 |
| | W: CA, JP, KR, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| PRAI | US 1992-878344 | | 19920504 | | |

OS MARPAT 120:38138

AB Pharmaceutical compns. and methods are provided for the colon-specific delivery of corticosteroids. Corticosteroids are administered in the form of prodrug conjugates with sugars which undergo reaction with enzymes produced by colonic microflora, thereby releasing the free drug. Dexamethasone Me acetyl glucuronate (prepn. given) was dissolved in methanolic NaOH followed by addn. of water and neutralization of the basic soln. to 7.5 with AcOH. The solvent was then removed and the residue was purified to obtain dexamethasone-.beta.-D-glucuronide (I). Serum ACTH level and I in rats with AcOH-induced colitis receiving 0.44.mu.mol/kg I/day orally was 447 and 3.8 as compared to 1246ng/mL and 8.5.mu.g/L, resp, for control.

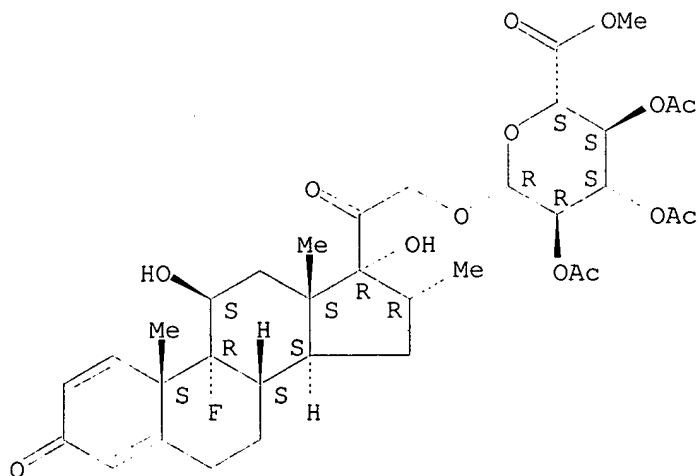
ST colonic delivery corticosteroid conjugate; dexamethasone glucuronide
colonic delivery

IT Intestine

(cecum, drug delivery to, corticosteroid conjugates for)

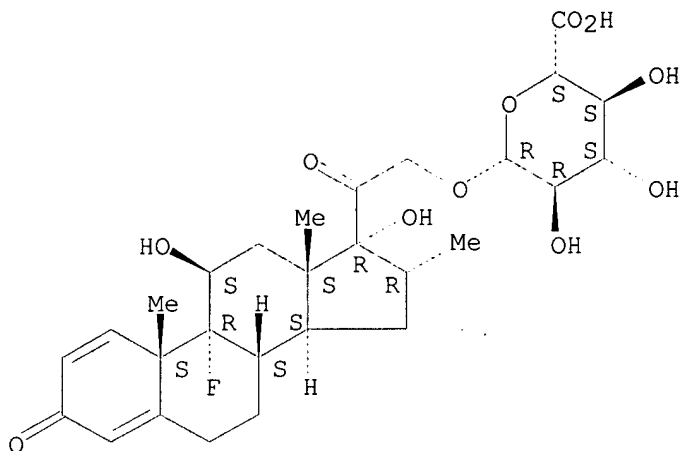
- IT Intestine
(colon, drug delivery to, corticosteroid conjugates for)
- IT Steroids, compounds
RL: PREP (Preparation)
(conjugates, prepn. of, for colonic delivery)
- IT Carbohydrates and Sugars, compounds
RL: PREP (Preparation)
(conjugates, with corticosteroids, prepn. of, for colonic delivery)
- IT Pharmaceutical dosage forms
(unit doses, corticosteroid conjugates with sugars in, for colonic delivery)
- IT 9033-06-1, Glucosidase
RL: RCT (Reactant); RACT (Reactant or reagent)
(corticosteroid conjugates hydrolysis by, in colon, for colonic delivery)
- IT **6804-44-0P** 152129-69-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)
- IT 50-02-2DP, Dexamethasone, conjugates with sugars 50-24-8DP, Prednisolone, conjugates with sugars 83-43-2DP, Methyl prednisolone, conjugates with sugars 378-44-9DP, Betamethasone, conjugates with sugars 3385-03-3DP, Flunisolide, conjugates with sugars 4419-39-0DP, Beclomethasone, conjugates with sugars 51333-22-3DP, Budesonide, conjugates with sugars 152129-70-9P **152154-28-4P**
RL: PREP (Preparation)
(prepn. of, for colonic delivery)
- IT 21085-72-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dexamethasone)
- IT 50-02-2, Dexamethasone 51333-22-3, Budesonide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with glucopyranoxyl bromide deriv.)
- IT **6804-44-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)
- RN 6804-44-0 HCAPLUS
- CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 152154-28-4P
 RL: PREP (Preparation)
 (prepn. of, for colonic delivery)
 RN 152154-28-4 HCAPLUS
 CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1994:37977 HCAPLUS

DN 120:37977

TI In vitro evaluation of dexamethasone-.beta.-D-glucuronide for colon-specific drug delivery

AU Haerberlin, Barbara; Rubas, Werner; Nolen, Harold W., III; Friend, David R.

CS Biomed. Polym. Dep., SRI Int., Menlo Park, CA, 94025, USA

SO Pharmaceutical Research (1993), 10(11), 1553-62

CODEN: PHREEB; ISSN: 0724-8741

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

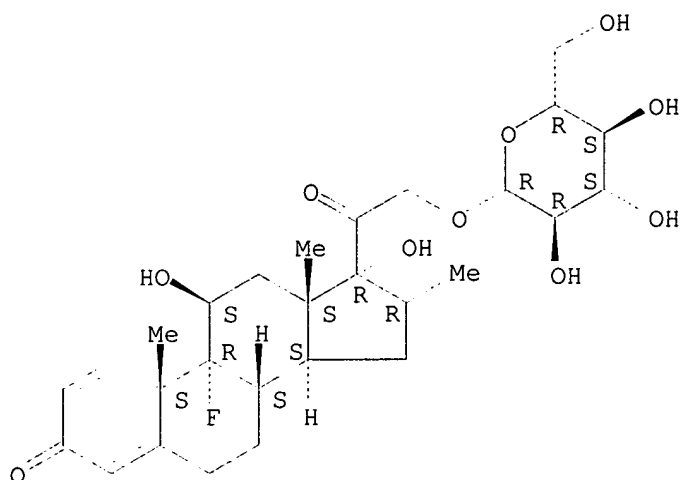
Section cross-reference(s): 1, 32, 33

AB Dexamethasone .beta.-D-glucuronide (I) is a potential prodrug for colonic delivery of the anti-inflammatory corticosteroid dexamethasone. Previous studies indicated that a glucoside prodrug of dexamethasone was susceptible to hydrolysis in the upper gastrointestinal tract. Resistance of I to hydrolysis in the upper gastrointestinal tract was therefore assessed. Conventional, germ-free, and colitic rats were used to examine enzyme levels along the gastrointestinal tract to compare the stability of 2 model substrates (p-nitrophenyl .beta.-D-glucoside and .beta.-D-glucuronide) and to evaluate the prodrug I. Hydrolytic activity was examd. in the luminal contents, mucosa, and underlying muscle/connective tissues in all three types of rats. Enzymic activity (.beta.-D-glucosidase and .beta.-D-glucuronidase) was greatest in the lumen of cecum and colon of conventional rats. In contrast, germ-free rats exhibited relatively high levels of .beta.-D-glucosidase activity (about 80% of total activity in the conventional rats) in the proximal small intestine and the distal small intestine. Rats with induced colitis (acetic acid) showed reduced levels of luminal .beta.-D-glucuronidase activity in the large intestine; however, .beta.-D-glucosidase activity was relatively unchanged relative to that of the convention rat. Mucosal .beta.-D-glucuronidase activity was significantly lower in the colitic rats compared with that in the conventional animals. Despite reduced luminal levels of .beta.-D-glucuronidase activity in the colitic rats,

there was still a sharp gradient of activity between the small and the large intestines. Permeability of the glucoside and glucuronide prodrugs of dexamethasone through a monolayer of Caco-2 cells was relatively low compared to that of dexamethasone. I should be relatively stable and poorly adsorbed in the upper gastrointestinal tract. Once the compd. reaches the large intestine, it should be hydrolyzed to dexamethasone and glucuronic acid. Specificity of colon delivery in humans should be even greater due to lower levels of .beta.-D-glucuronidase activity in the small intestine compared with that in the lab. rat.

ST dexamethasone glucuronide colon delivery prepn
 IT Hydrolysis
 (of dexamethasone glucuronide, colon-specific drug delivery in relation to)
 IT Intestine
 (colon, dexamethasone glucuronide delivery to, as prodrug, evaluation of)
 IT Intestine, metabolism
 (large, dexamethasone glucuronide absorption by, drug delivery in relation to)
 IT Intestine, metabolism
 (mucosa, dexamethasone glucuronide absorption by, drug delivery in relation to)
 IT Intestine, metabolism
 (small, dexamethasone glucuronide absorption by, drug delivery in relation to)
 IT 9001-22-3, .beta.-D-Glucosidase 9001-45-0, .beta.-D-Glucuronidase
 RL: BIOL (Biological study)
 (dexamethasone glucuronide hydrolysis by, colon-specific drug delivery in relation to)
 IT 2492-87-7 10344-94-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (hydrolysis of, dexamethasone glucuronide colon-specific drug delivery in relation to)
 IT 88158-43-4 105088-08-2
 RL: PRP (Properties)
 (physicochem. properties and permeability of, dexamethasone glucuronide colon-specific drug delivery in relation to)
 IT 6804-44-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. and deprotection of)
 IT 152154-28-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and in vitro evaluation of, for colon-specific drug delivery)
 IT 50-02-2, Dexamethasone
 RL: BIOL (Biological study)
 (prodrugs for, glucuronide deriv. as, prepn. and in vitro evaluation of, for colon-specific drug delivery)
 IT 21085-72-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with dexamethasone)
 IT 88158-43-4 105088-08-2
 RL: PRP (Properties)
 (physicochem. properties and permeability of, dexamethasone glucuronide colon-specific drug delivery in relation to)
 RN 88158-43-4 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

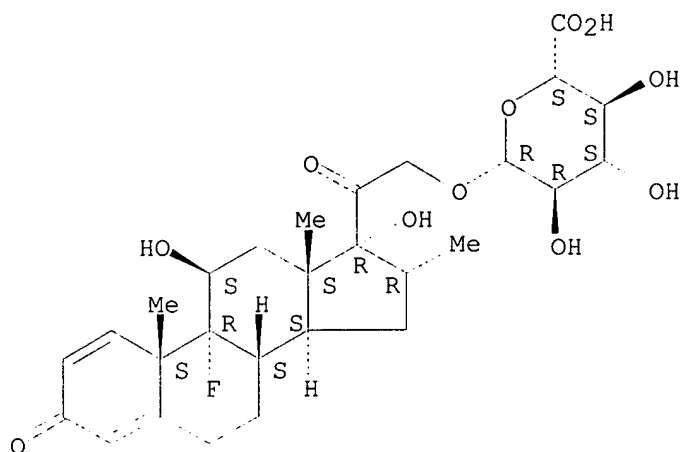
Absolute stereochemistry.



RN 105088-08-2 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, monosodium salt (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



● Na

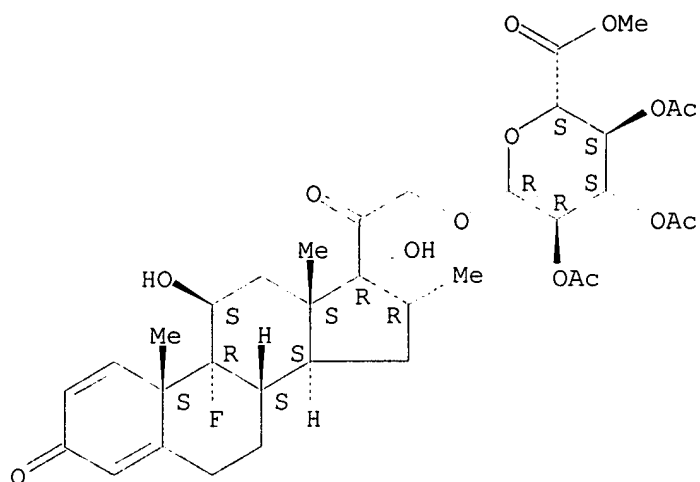
IT 6804-44-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and deprotection of)

RN 6804-44-0 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester,
2,3,4-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



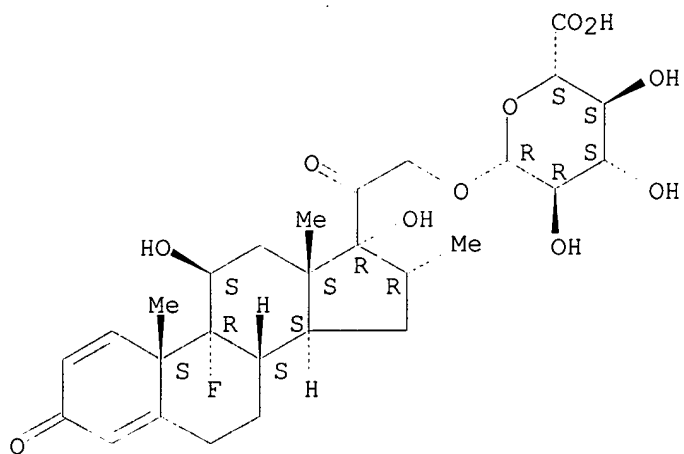
IT 152154-28-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and in vitro evaluation of, for colon-specific drug delivery)

RN 152154-28-4 HCAPLUS

CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:240666 HCAPLUS

DN 118:240666

TI Relative **antiinflammatory** effect of oral dexamethasone-.beta.-D-glucoside and dexamethasone in experimental IBD

AU Friend, D.; Phillips, S.; McLeod, A.; Tozer, T. N.

CS Biopharm. Res. Group, SRI Int., Menlo Park, CA, 94025, USA

SO Proc. Program Int. Symp. Controlled Release Bioact. Mater., 18th (1991), 564-5. Editor(s): Kellaway, Ian W. Publisher: Controlled Release Soc., Deerfield, Ill.

CODEN: 58GMAH

DT Conference

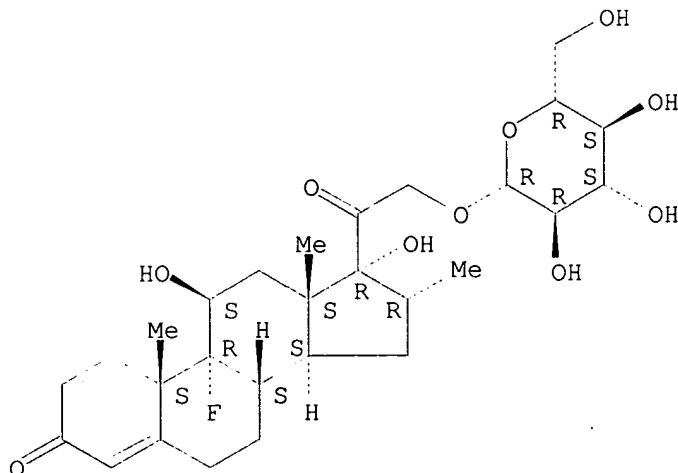
LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

- AB The relative anti-**inflammatory** effect of dexamethasone and a prodrug, dexamethasone-.beta.-D-glucoside, was assessed in guinea-pigs with exptl.-induced **inflammatory** bowel disease (IBD). The glucoside prodrug is designed to reach the large intestine following oral administration. The active agent is liberated when the prodrug is hydrolyzed by glycosidases of colonic bacteria. Guinea-pigs were administered degraded carrageenan in their drinking water to produce exptl. IBD. Starting on day 15, dexamethasone (1.3 .mu.mol/kg) or dexamethasone-.beta.-D-glucoside (1.3 or 0.65 .mu.mol/kg) was administered by gastric intubation once daily for 5 days. Relative to control animals, the drug and prodrug treatments reduced the total no. of cecal ulcers. While there was no difference statistically between the drug and prodrug treatments, the data suggest that a lower dose of dexamethasone, administered as its glucoside prodrug, could reduce side-effects without reduced efficacy. Thus, localized delivery of dexamethasone to the large bowel can improve pharmacotherapy of IBD by reducing the side-effects assocd. with corticosteroids.
- ST dexamethasone prodrug **inflammatory** bowel disease
- IT Intestine, disease or disorder
(**inflammatory**, treatment of, with dexamethasone and dexamethasone prodrug)
- IT **88158-43-4**
RL: BIOL (Biological study)
(**inflammatory** bowel disease treatment with)
- IT 50-02-2, Dexamethasone
RL: BIOL (Biological study)
(**inflammatory** bowel disease treatment with, prodrug in relation to)
- IT **88158-43-4**
RL: BIOL (Biological study)
(**inflammatory** bowel disease treatment with)
- RN 88158-43-4 HCAPLUS
- CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1991:214302 HCAPLUS

DN 114:214302

TI Colon-specific delivery of dexamethasone from a glucoside prodrug in the guinea pig

AU Tozer, Thomas N.; Rigod, Jean; McLeod, Andrew D.; Gungon, Ramon; Hoag, M.

Kim; Friend, David R.

CS Sch. Pharm., Univ. California, San Francisco, CA, 94143-0446, USA

SO Pharmaceutical Research (1991), 8(4), 445-54

CODEN: PHREEB; ISSN: 0724-8741

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

AB Dexamethasone-21.beta.-D-glucoside (I) is a potential prodrug for colonic delivery of the anti-inflammatory agent, dexamethasone. The ability of this prodrug to deliver dexamethasone selectively to the colon depends not only on its being slowly absorbed from the alimentary canal, but also on its having chem. and enzymic stability in the stomach and small intestine. Once reaching the large bowel, it should be quant. hydrolyzed to release the active agent. The potential of I for colon-specific delivery of dexamethasone is assessed by detg. the rates of its hydrolysis down the alimentary canal of the guinea pig, an animal in which an inflammatory bowel disease model has been developed. The hydrolytic activity is examd. in tissues and luminal contents of the stomach, proximal and distal segments of the small intestine, cecum, and colon. For the tissues, the greatest hydrolytic activity is in the proximal small intestine, while the stomach, cecum, and colon have only moderate activity. In contrast, the contents of the cecum and colon show greater activity than the contents of the small intestine and stomach. The luminal contents retained .beta.-glucosidase activity even after repeated centrifugation and resuspension in a buffer. The activity was unaffected by homogenization. These observations suggest that hydrolytic activity is assocd. with enzymes located on the surface of luminal cells. The movement and hydrolysis of I down the gastrointestinal tract of the guinea pig are also examd. About 20-30% of an oral dose appears to reach the cecum. Here the prodrug is rapidly hydrolyzed to the active drug. From i.v. administration of the prodrug and drug, it is apparent that I is poorly absorbed in the gastrointestinal tract (bioavailability, <1%). There is a ninefold selective advantage for delivery of dexamethasone in cecal tissues in the guinea pig under the conditions of this expt. Thus, there is a potential for a decrease in the usual dose and a concomitant redn. in the systemic exposure to dexamethasone. Because humans have much less glucosidase activity in the small intestine, even greater site-selective delivery to the cecum and colon is expected.

ST dexamethasone colon delivery glucoside prodrug

IT Drug bioavailability

(of dexamethasone, oral, from glucoside prodrug)

IT Intestine, metabolism

(cecum, dexamethasone glucoside hydrolysis in, in drug delivery)

IT Intestine, metabolism

(colon, dexamethasone glucoside hydrolysis in, in drug delivery)

IT Pharmaceutical dosage forms

(prodrugs, of dexamethasone, glucoside as, for drug colon delivery)

IT Intestine, metabolism

(small, dexamethasone glucoside hydrolysis in, in drug delivery)

IT 88158-44-5

RL: BIOL (Biological study)

(colon delivery of, as prodrug)

IT 50-02-2, Dexamethasone

RL: BIOL (Biological study)

(colon delivery of, glucoside prodrug for)

IT 9001-22-3

RL: BIOL (Biological study)

(dexamethasone glucoside hydrolysis by, as prodrug, colon delivery in relation to)

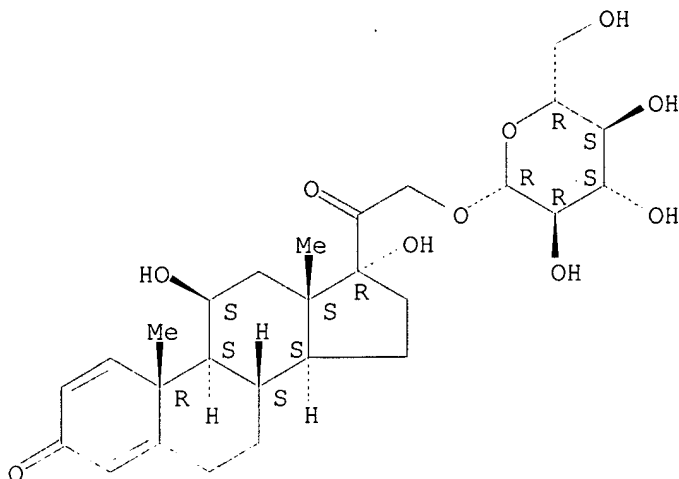
IT 88158-44-5

RL: BIOL (Biological study)

(colon delivery of, as prodrug)

RN 88158-44-5 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1991:192367 HCAPLUS
 DN 114:192367
 TI Effect of antibiotic pretreatment on glycoside/glycosidase-based colonic drug delivery
 AU Friend, David R.; Chow, Joseph J.; Chang, George W.
 CS Controlled Release Biomed. Polym. Dep., SRI Int., Menlo Park, CA, 94025, USA
 SO Drug Design and Delivery (1990), 6(4), 311-18
 CODEN: DDDEEJ; ISSN: 0884-2884
 DT Journal
 LA English
 CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 1
 AB The effect of antibiotic pretreatment on the intestinal distribution and hydrolysis of the prodrug prednisolone .beta.-D-glucoside was studied in rats. A combination of neomycin, lincomycin, and metronidazole was administered twice daily by gastric intubation for 3 days to young adult male rats. On the fourth day, prednisolone .beta.-D-glucoside was administered intragastrically. The distribution of prodrug and drug in the intestinal contents was significantly altered by the antibiotic treatment. In comparison with untreated rats, stomach to cecum transit time appeared to be reduced, and more prodrug was hydrolyzed in the small intestine. In addn., an appreciable amt. of the dose was retained longer in the small intestine of treated animals. The total recovery of prodrug and drug was unaltered by the pretreatment. Possible explanations for the obsd. results are presented.
 ST colon drug delivery antibiotic; prednisolone glucoside prodrug colon delivery
 IT Pharmaceutical dosage forms
 (for delivery to colon, antibiotics effect on prednisolone glucoside prodrug absorption by intestine in relation to)
 IT Intestine, metabolism
 (prednisolone glucoside prodrug absorption by, antibiotics effect on, drug delivery to colon in relation to)
 IT Antibiotics
 (prednisolone glucoside prodrug distribution and hydrolysis in

intestine response to, colon delivery in relation to)

IT Intestine
(colon, drug delivery to, antibiotics effect on prednisolone glucoside prodrug absorption in relation to)

IT 154-21-2, Lincomycin 443-48-1, Metronidazole 1404-04-2, Neomycin
RL: BIOL (Biological study)
(prednisolone glucoside prodrug distribution and hydrolysis in intestine response to, colon delivery in relation to)

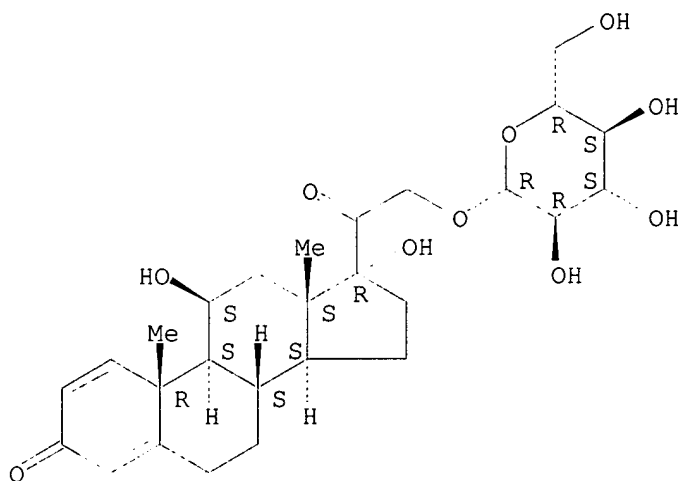
IT **88158-44-5**
RL: BIOL (Biological study)
(prodrug, for delivery to colon, antibiotics effect on)

IT **88158-44-5**
RL: BIOL (Biological study)
(prodrug, for delivery to colon, antibiotics effect on)

RN 88158-44-5 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1991:171170 HCAPLUS

DN 114:171170

TI Colon-specific drug delivery from a glucoside prodrug in the guinea pig.
Efficacy study

AU Friend, David R.; Phillips, Sandra; Tozer, Thomas N.

CS Biopharm. Res. Group, SRI Int., Menlo Park, CA, 94025, USA

SO Journal of Controlled Release (1991), 15(1), 47-54
CODEN: JCREEC; ISSN: 0168-3659

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

AB The effect of a prodrug-based colonic delivery system on carrageenan-induced **inflammatory** bowel disease (IBD) in guinea-pigs was investigated. Guinea-pigs were administered 4 wt.% of degraded carrageenan in the drinking water for 2 wk to induce exptl. IBD. The prodrug, dexamethasone-.beta.-D-glucoside, was then administered at one of two dose levels (1.3 or 0.65 .mu.mol/kg) once daily by gastric intubation for 5 days; dexamethasone (1.3 .mu.mol/kg) was also administered in the same manner. The higher dose of dexamethasone-.beta.-D-glucoside led to reduced gross pathol. effects (fluid cecal contents, redness, edema, ulcerations), and a significantly lower histopathol. score relative to dexamethasone, which was ineffective at controlling the

inflammatory response relative to control animals. The lower dose of prodrug was somewhat more effective than dexamethasone or no drug treatment in controlling gross pathol. effects of the large intestine, but was ineffective when evaluated histol. The implications of these findings are discussed.

ST dexamethasone glucoside prodrug colon delivery; **inflammatory**
bowel disease dexamethasone prodrug

IT Intestine
(colon, dexamethasone glucoside prodrug for delivery to, in
inflammatory bowel disease)

IT Intestine, disease or disorder
(**inflammatory**, dexamethasone glucoside prodrug for delivery
to colon in)

IT Pharmaceutical dosage forms
(oral, dexamethasone glucoside prodrug for colon-specific delivery
from, in **inflammatory** bowel disease)

IT 50-02-2, Dexamethasone
RL: BIOL (Biological study)
(glucoside prodrug for colon-specific delivery of, in
inflammatory bowel disease)

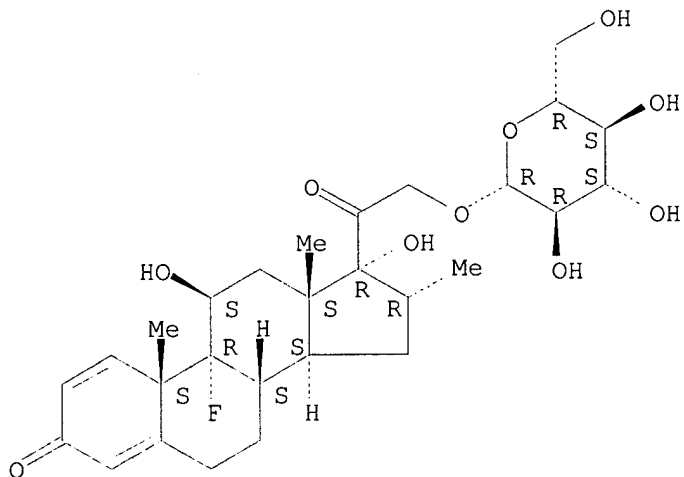
IT **88158-43-4**
RL: BIOL (Biological study)
(prodrug, for colon-specific delivery, in **inflammatory** bowel
disease)

IT **88158-43-4**
RL: BIOL (Biological study)
(prodrug, for colon-specific delivery, in **inflammatory** bowel
disease)

RN 88158-43-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-
11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1985:100803 HCAPLUS

DN 102:100803

TI Colon-specific steroidal glycoside prodrugs

IN Friend, David Robert; Chang, George Washington

PA University of California, Berkeley, USA

SO Eur. Pat. Appl., 70 pp.
CODEN: EPXXDW

DT Patent

LA English
 IC A61K031-70; A61K031-705; C07J017-00
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 2, 32, 33

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | EP 123485 | A1 | 19841031 | EP 1984-302549 | 19840413 |
| | R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| | WO 8404041 | A1 | 19841025 | WO 1984-US554 | 19840410 |
| | W: JP | | | | |
| | JP 60501105 | T2 | 19850718 | JP 1984-502049 | 19840410 |
| PRAI | US 1983-484983 | | 19830414 | | |
| | US 1984-593492 | | 19840329 | | |
| | WO 1984-US554 | | 19840410 | | |

AB A colon-specific producing delivery system is based on the use of a steroidal glycoside prodrug compn. which undergoes reaction in vivo with glycosidases produced by colon microflora to release a drug capable of being absorbed the intestinal mucosa. Dexamethasone [50-02-2], prednisolone [50-24-8], hydrocortisone [50-23-7], and fludrocortisone [127-31-1] are used as the steroidal substrates. Thus, dexamethasone 21-.beta.-D-glucoside (I) [88158-43-4] and prednisolone 21-.beta.-D-glucoside (II) [88158-44-5] were prepd. by the glycosylation of dexamethasone and prednisolone, resp., by using a modified Koenigs-Knoss reaction. 2,3,4,6-Tetra-O-acetyl-1-bromo-.alpha.-D-glucopyranose [572-09-8] was coupled with the appropriate steroid in CCl4 in the presence of Ag2CO3 and the acetyl glycosides formed were treated with 0.01N NaOH eliminating the acetyl groups to yield the resp. glucosides. The recovery of glucosides and free steroids from the small intestine and cecum at various times following the oral administration of I and II were detd. At 4 h, 59% of administered I was recovered unhydrolyzed. The delivery of II was less efficient than that of I. Only 14.8% of the administered dose of II could be recovered as such from the lower small intestine after 4 h.

ST glycoside steroid prodrug colon; prednisolone prodrug colon; dexamethasone prodrug colon; hydrolysis steroid glycoside prodrug

IT Hydrolysis

Kinetics of hydrolysis

(of steroidal glycoside prodrugs, colon delivery in relation to)

IT Intestine, metabolism

(colon, steroidal glycoside prodrugs delivery to)

IT Glycosides

RL: BIOL (Biological study)

(steroidal, prodrugs, for delivery to colon)

IT 5346-90-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(bromination of)

IT 88158-45-6P 88179-95-7P 92901-28-5P

92901-29-6P 92901-30-9P 92901-31-0P

92901-32-1P 92901-33-2P 92937-53-6P

RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and deacetylation of)

IT 88158-43-4P 88158-44-5P 92901-21-8P

92901-22-9P 92901-23-0P 92901-24-1P

92901-25-2P 92901-26-3P 92901-27-4P

RL: PREP (Preparation)

(prepn. of, as prodrug for delivery to colon)

IT 2492-87-7 3482-57-3 7493-95-0

RL: BIOL (Biological study)

(prodrug model, hydrolysis of)

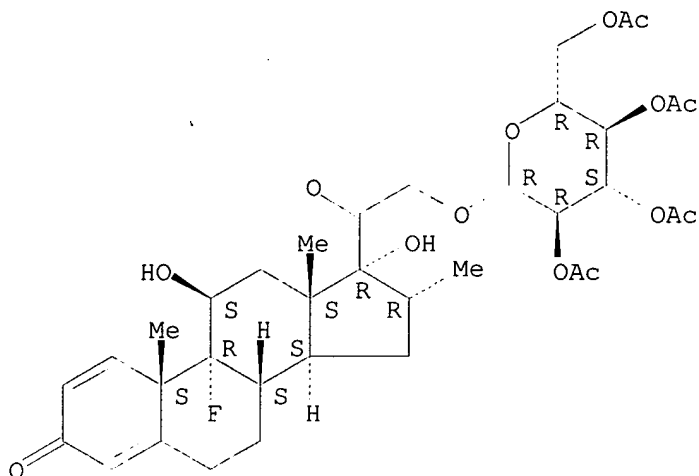
IT 50-02-2 50-23-7 50-24-8 127-31-1

RL: BIOL (Biological study)

(prodrugs for, glycosides as, delivery of, to colon)

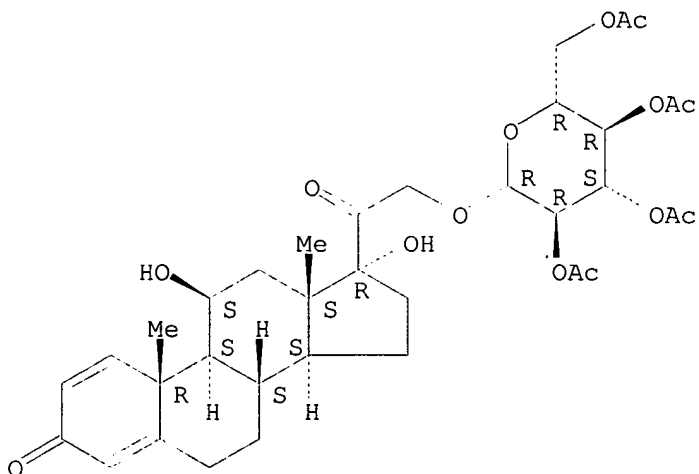
IT 572-09-8 3068-32-4 14227-66-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with steroids)
 IT 88158-45-6P 88179-95-7P 92901-28-5P
 92901-29-6P 92901-30-9P 92901-31-0P
 92901-32-1P 92901-33-2P 92937-53-6P
 RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. and deacetylation of)
 RN 88158-45-6 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-
 [(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-,
 (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

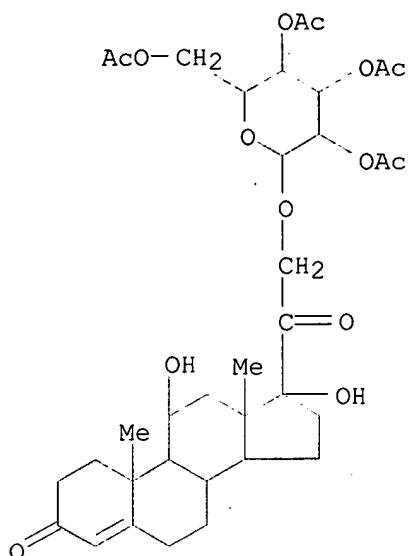


RN 88179-95-7 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

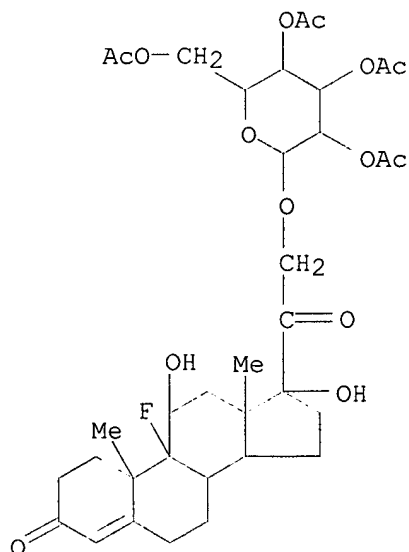
Absolute stereochemistry.



RN 92901-28-5 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

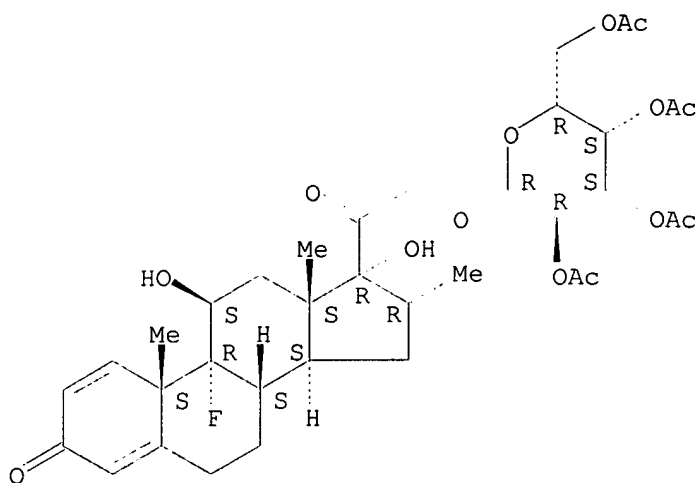


RN 92901-29-6 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 9-fluoro-11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)



RN 92901-30-9 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

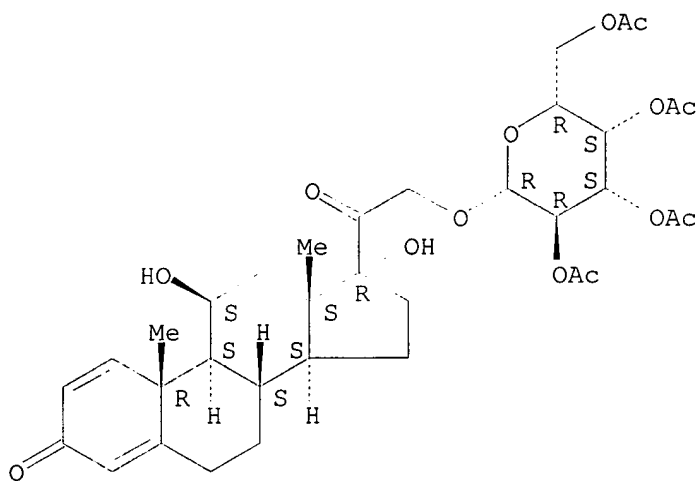
Absolute stereochemistry.



RN 92901-31-0 HCAPLUS

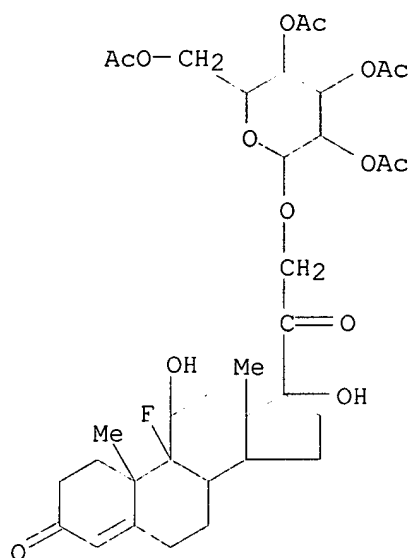
CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



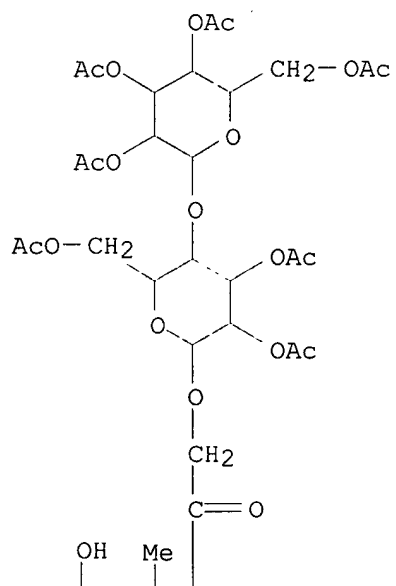
RN 92901-32-1 HCAPLUS

CN Pregn-4-ene-3,20-dione, 9-fluoro-11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

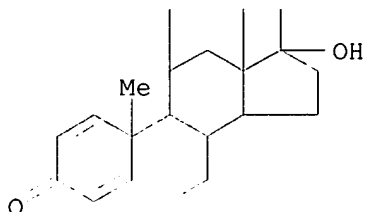


RN 92901-33-2 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[[2,3,6-tri-O-acetyl-4-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)-.beta.-D-glucopyranosyl]oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

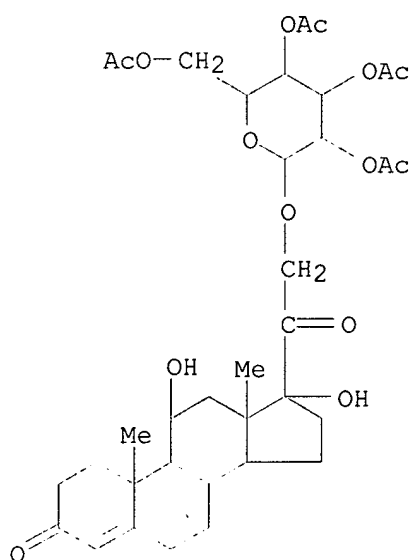
PAGE 1-A



PAGE 2-A



RN 92937-53-6 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)



IT 88158-43-4P 88158-44-5P 92901-21-8P
 92901-22-9P 92901-23-0P 92901-24-1P
 92901-25-2P 92901-26-3P 92901-27-4P

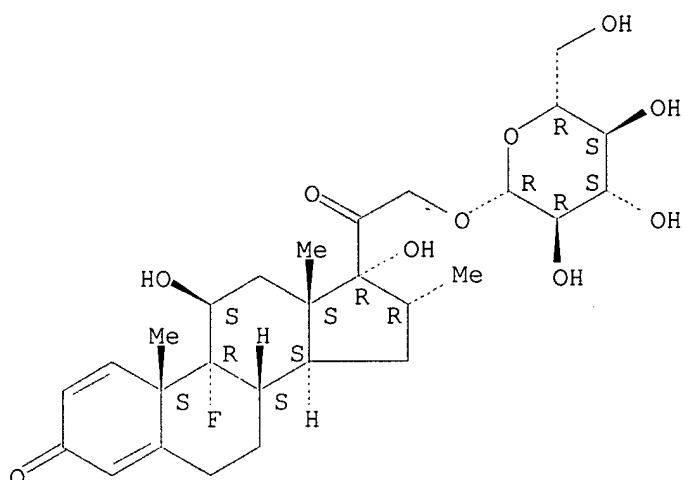
RL: PREP (Preparation)

(prepn. of, as prodrug for delivery to colon)

RN 88158-43-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

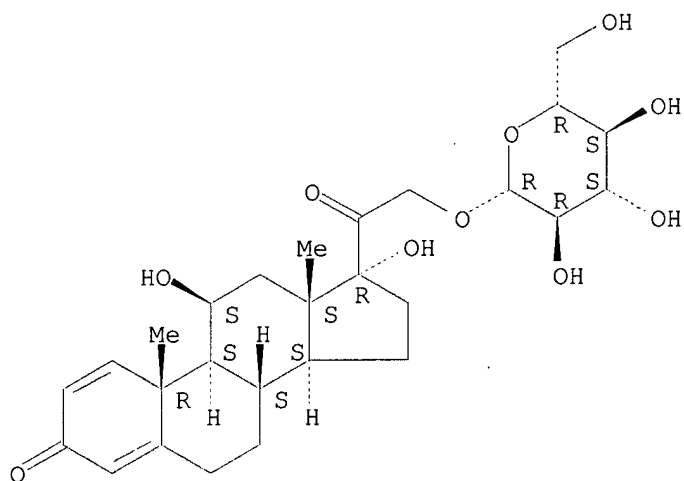
Absolute stereochemistry.



RN 88158-44-5 HCAPLUS

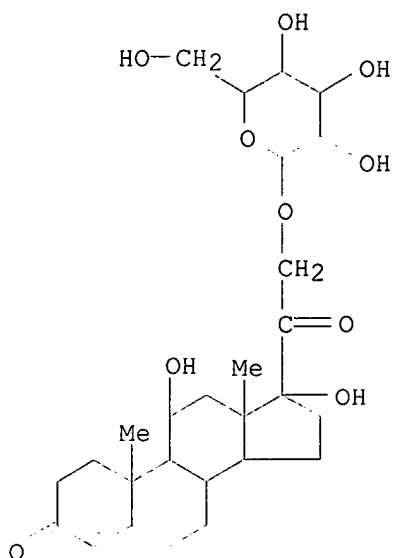
CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

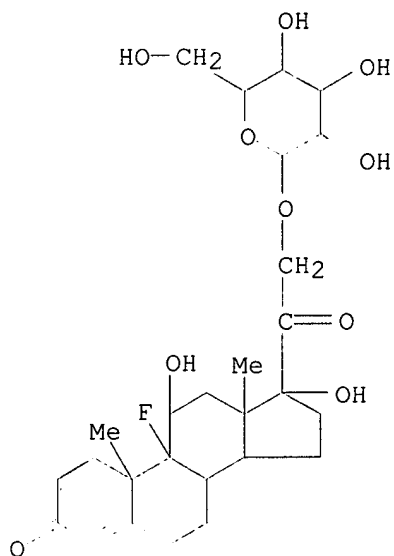


RN 92901-21-8 HCAPLUS

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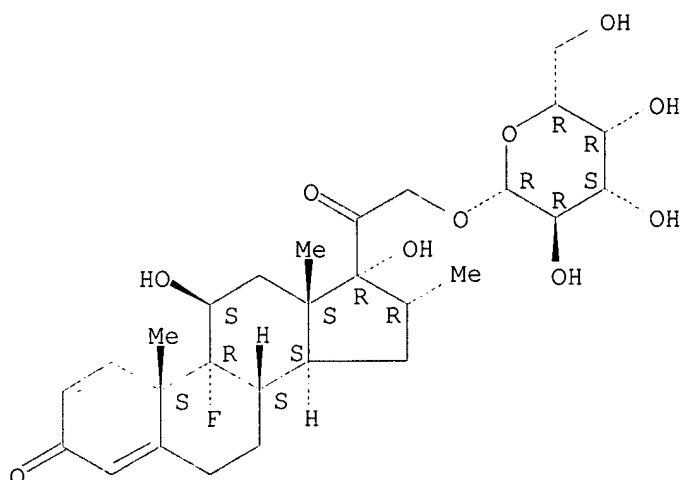


RN 92901-22-9 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)



RN 92901-23-0 HCAPLUS
 CN Pregn-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

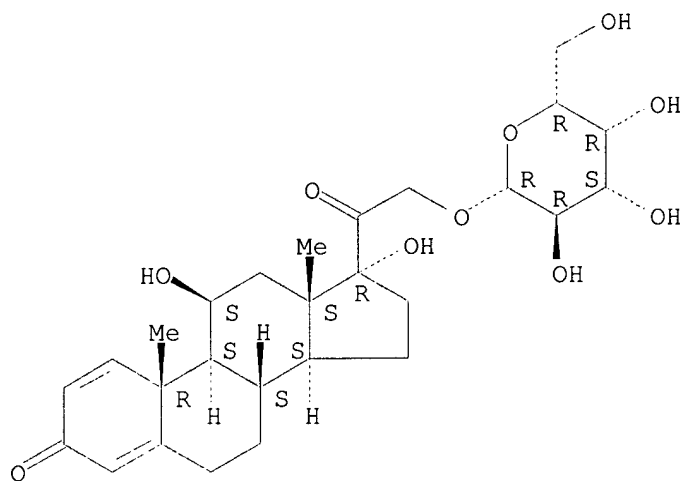
Absolute stereochemistry.



RN 92901-24-1 HCAPLUS

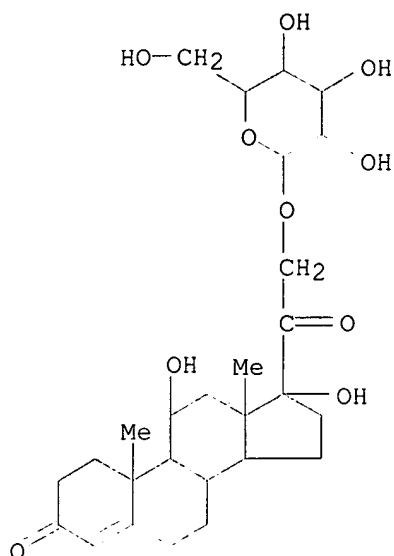
CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

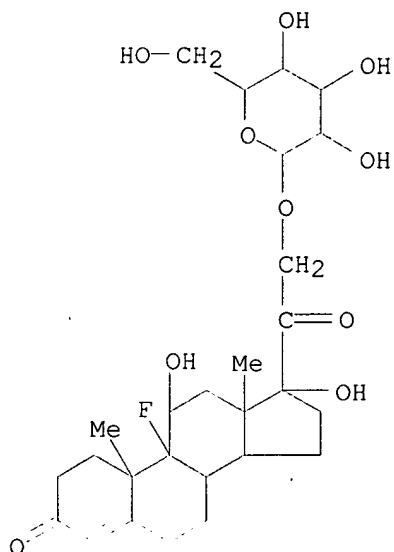


RN 92901-25-2 HCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

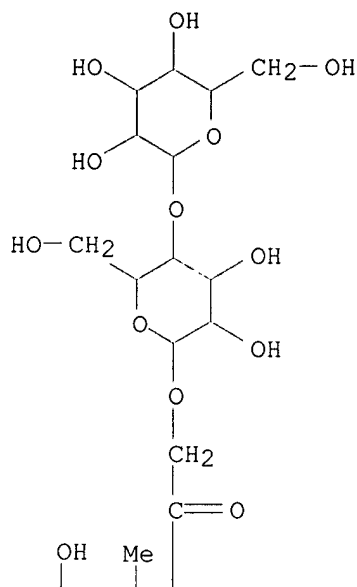


RN 92901-26-3 HCAPLUS
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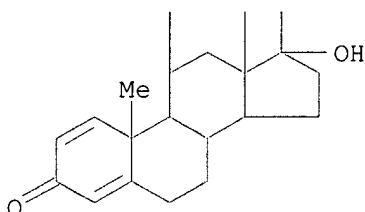


RN 92901-27-4 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 21-[(4-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

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L103 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1985:32032 HCAPLUS

DN 102:32032

TI Drug glycosides: potential prodrugs for colon-specific drug delivery

AU Friend, David R.; Chang, George W.

CS Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA

SO Journal of Medicinal Chemistry (1985), 28(1), 51-7

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 2, 32

AB The 21-yl .beta.-D-glucosides and galactosides of dexamethasone, prednisolone, hydrocortisone, and fludrocortisone and prednisolone-21-yl .beta.-D-cellobioside [92901-27-4] were prepd. by a modified Koenigs-Knorr reaction. The deacetylated glycoside prodrugs, along with the p-nitrophenyl derivs. of .beta.-D-glucoside, galactoside, and cellobioside, were subjected to hydrolysis by the contents of the rat stomach, proximal small intestine (PSI), distal small intestine (DSI), and cecum. All the prodrugs were hydrolyzed slowly by PSI and stomach

contents, more rapidly by contents of the DSI, and most rapidly by cecal contents. Hydrolysis rates catalyzed by DSI contents decreased in the following order: prednisolone-21-yl .beta.-D-galactoside [92901-24-1] > prednisolone-21-yl .beta.-D-glucoside [88158-44-5] > prednisolone-21-yl .beta.-D-cellobioside > dexamethasone-21-yl .beta.-D-galactoside [92901-23-0] > dexamethasone-21-yl .beta.-D-glucoside [88158-43-4]. Hydrolysis of the prednisolone cellobioside was only 1/2 that of glucoside and 1/4 that of the galactoside. Hydrolysis of all the prodrugs in cecal contents was rapid, with the exceptions of hydrocortisone-21-yl .beta.-D-glucoside [92901-21-8] and fludrocortisone-21-yl .beta.-D-glucoside [92901-22-9], which were hydrolyzed more slowly than the other glucoside prodrugs. Eadie-Hofstee plots for hydrolysis of the glucoside compds. suggested that bacterial .beta.-D-glucosidase [9001-22-3] activity in the colon may be more heterogeneous in nature than .beta.-D-galactosidase [9031-11-2] activity. The logarithm of the partition coeff. (octanol-buffer) of the cellobioside (-0.56) was considerably lower than that of the other prodrugs, which ranged from 0.11 to 0.84; comparative detns. for the free steroids ranged from 1.54 to 1.73. These relative rates of hydrolysis and relative lipophilicities, along with previously reported animal expts., enable one to est. the site specificity of glycoside prodrugs prior to extensive animal studies.

- ST steroid glycoside prodrug prepn; drug glycoside colon specific delivery
- IT Lipophilicity
 - (of steroid glycoside prodrugs)
- IT Kinetics of hydrolysis
 - (of steroid glycoside prodrugs by gastrointestinal contents)
- IT Intestinal content
 - Stomach content
 - (steroid glycoside prodrugs hydrolysis by)
- IT Intestine, metabolism
 - (colon, prodrugs specific for)
- IT Pharmaceuticals
 - (prodrugs, glycosides as)
- IT Glycosides
 - RL: SPN (Synthetic preparation); PREP (Preparation)
 - (steroidal, prepn. of, as colon-specific prodrugs, hydrolysis by gastrointestinal contents and lipophilicity in relation to)
- IT 50-02-2 50-23-7 50-24-8 127-31-1
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (Koenigs-Knorr reaction of, with acetylbromosugars)
- IT 572-09-8 3068-32-4
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (Koenigs-Knorr reaction of, with steroids)
- IT 88158-43-4 88158-44-5
 - RL: BIOL (Biological study)
 - (colon-specific prodrug, hydrolysis by gastrointestinal contents and lipophilicity in relation to)
- IT 9001-22-3 9031-11-2
 - RL: BIOL (Biological study)
 - (of intestine, steroid glycoside prodrugs hydrolysis by bacterial)
- IT 14227-66-8P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 - (prepn. and Koenigs-Knorr reaction of, with prednisolone)
- IT 92901-28-5P 92901-29-6P 92901-30-9P
 92901-31-0P 92901-32-1P 92901-33-2P
 92937-53-6P
 - RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 - (prepn. and hydrolysis of)
- IT 92901-21-8P 92901-22-9P 92901-23-0P

92901-24-1P 92901-25-2P 92901-26-3P

92901-27-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as colon-specific prodrug, hydrolysis by gastrointestinal contents and lipophilicity in relation to)

IT 88158-43-4 88158-44-5

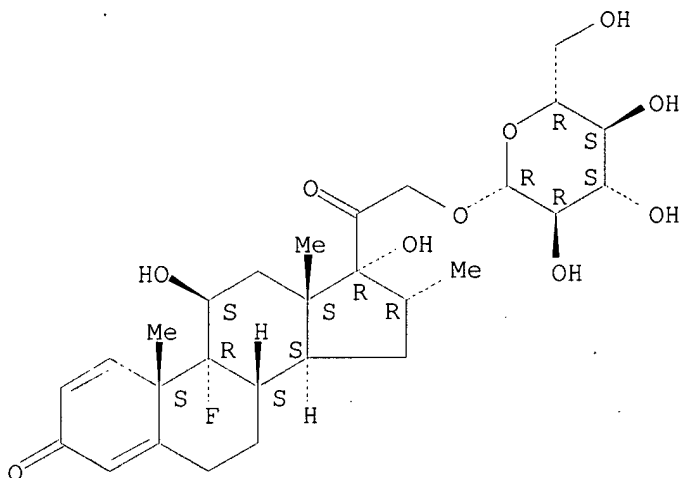
RL: BIOL (Biological study)

(colon-specific prodrug, hydrolysis by gastrointestinal contents and lipophilicity in relation to)

RN 88158-43-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

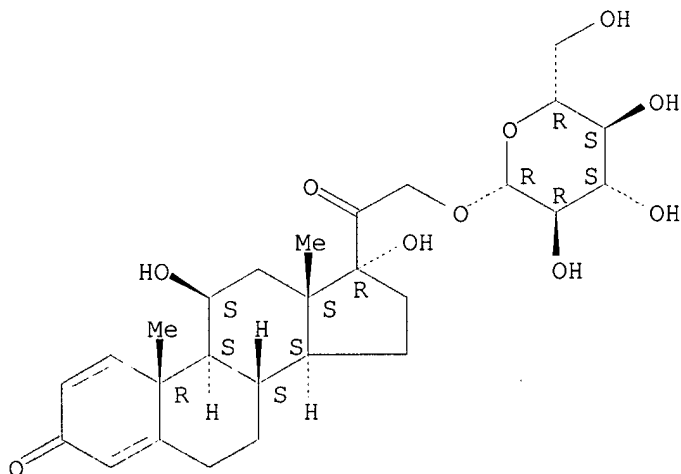
Absolute stereochemistry.



RN 88158-44-5 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 92901-28-5P 92901-29-6P 92901-30-9P

92901-31-0P 92901-32-1P 92901-33-2P

92937-53-6P

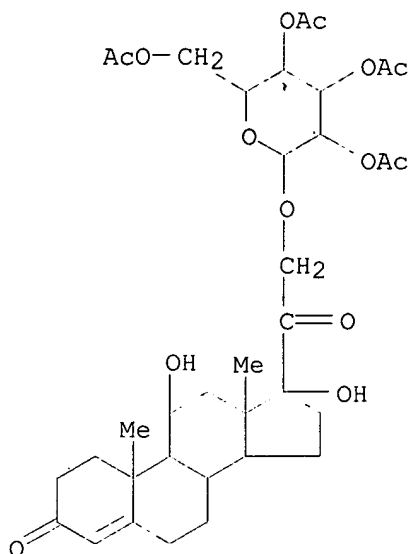
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(prepn. and hydrolysis of)

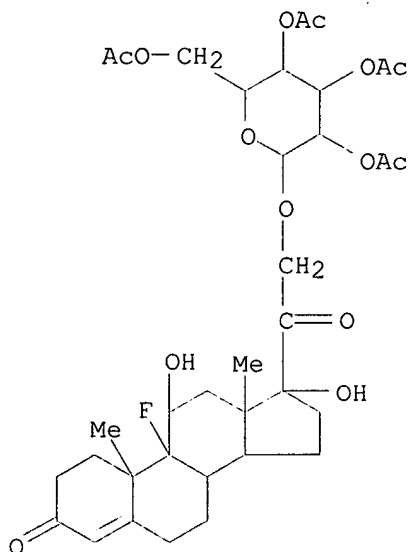
RN 92901-28-5 HCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)



RN 92901-29-6 HCAPLUS

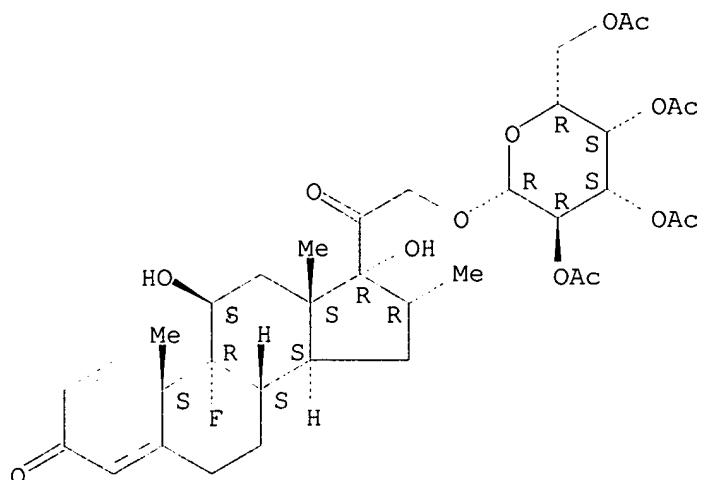
CN Pregn-4-ene-3,20-dione, 9-fluoro-11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)



RN 92901-30-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

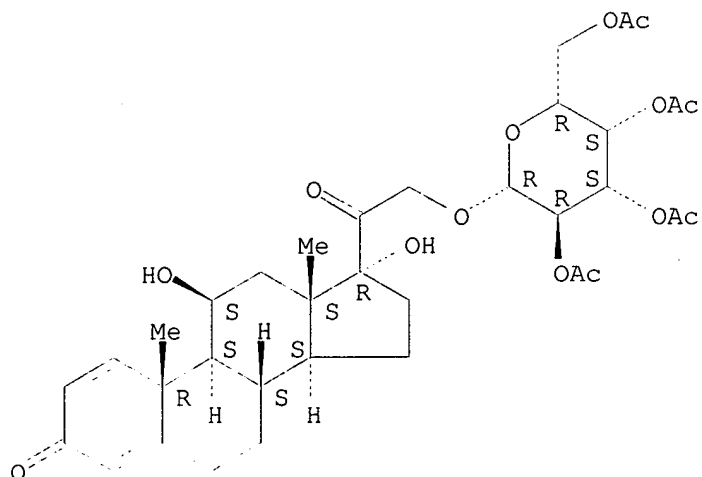
Absolute stereochemistry.



RN 92901-31-0 HCAPLUS

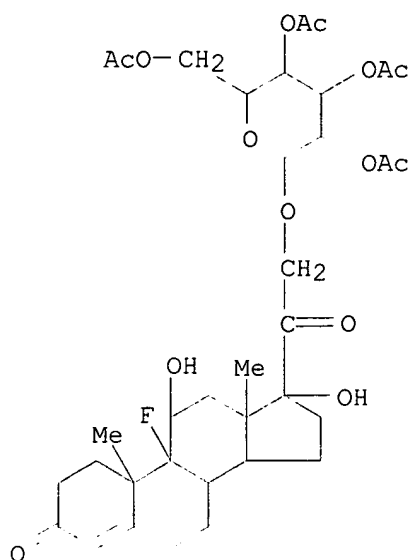
CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



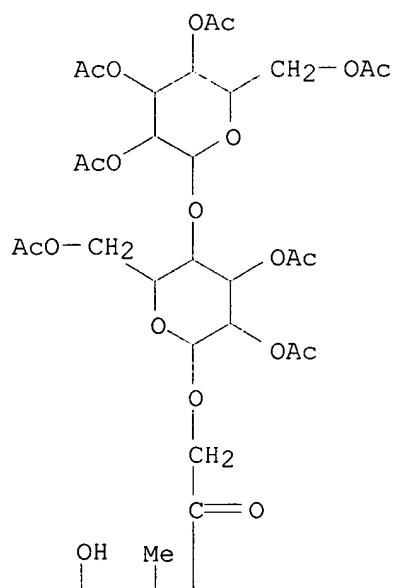
RN 92901-32-1 HCAPLUS

CN Pregna-4-ene-3,20-dione, 9-fluoro-11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

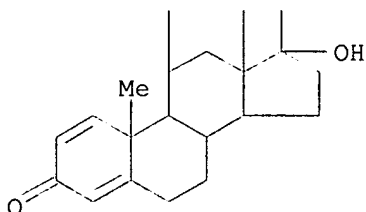


RN 92901-33-2 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[[2,3,6-tri-O-acetyl-4-(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)-.beta.-D-glucopyranosyl]oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

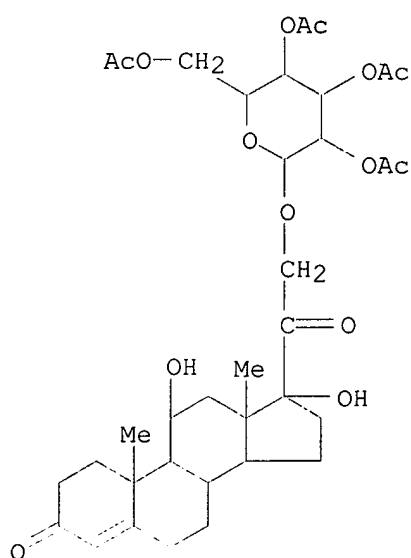
PAGE 1-A



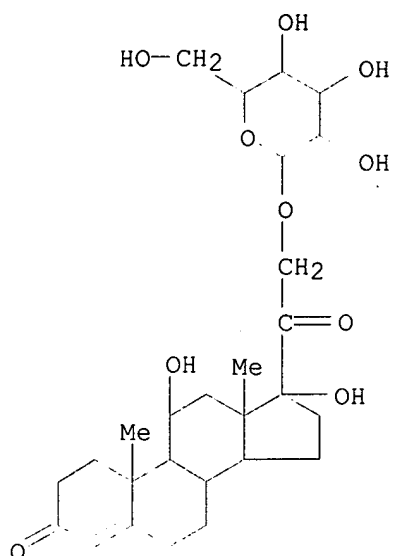
PAGE 2-A



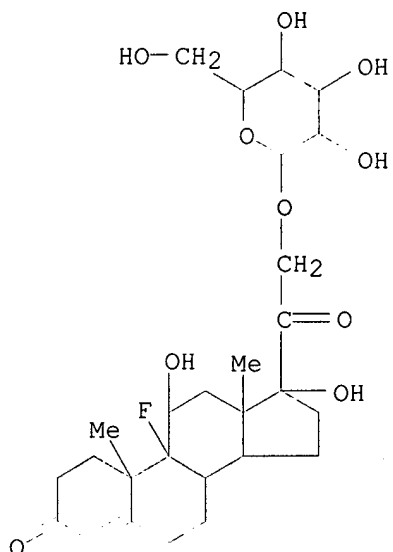
RN 92937-53-6 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)



IT 92901-21-8P 92901-22-9P 92901-23-0P
 92901-24-1P 92901-25-2P 92901-26-3P
 92901-27-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as colon-specific prodrug, hydrolysis by gastrointestinal
 contents and lipophilicity in relation to)
 RN 92901-21-8 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-,
 (11.beta.)- (9CI) (CA INDEX NAME)

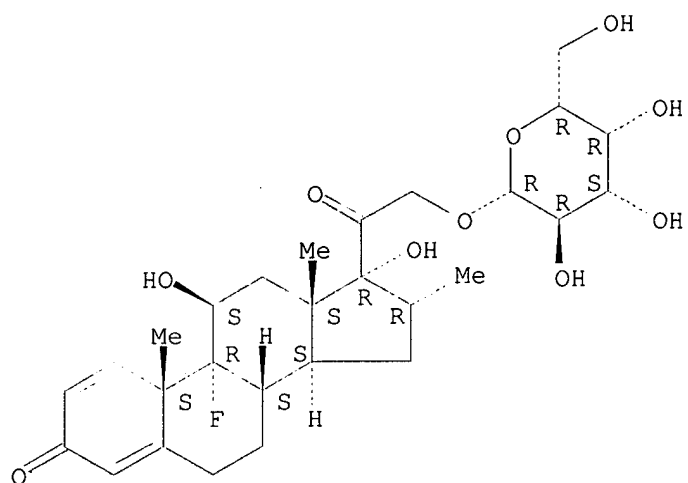


RN 92901-22-9 HCAPLUS
 CN Pregn-4-ene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)



RN 92901-23-0 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

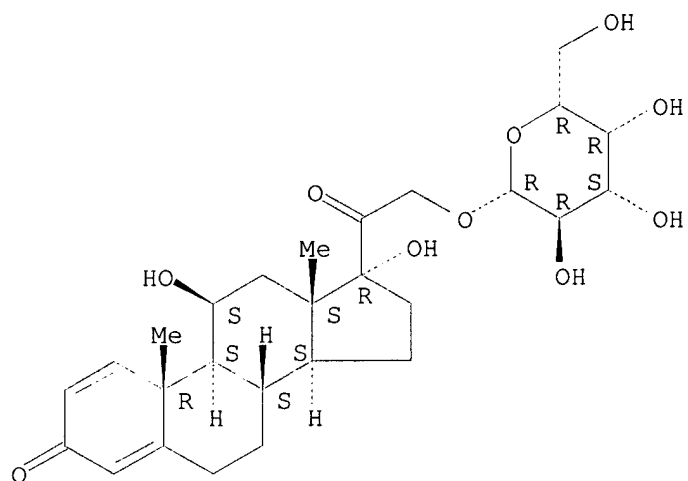
Absolute stereochemistry.



RN 92901-24-1 HCAPLUS

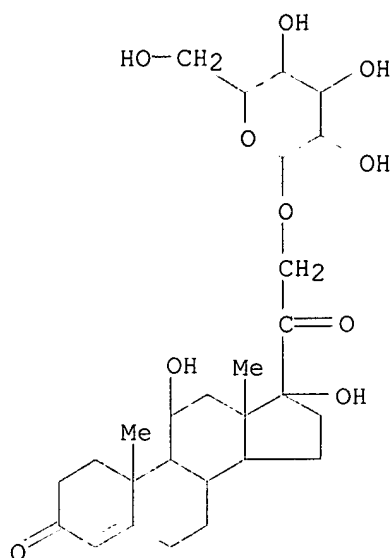
CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



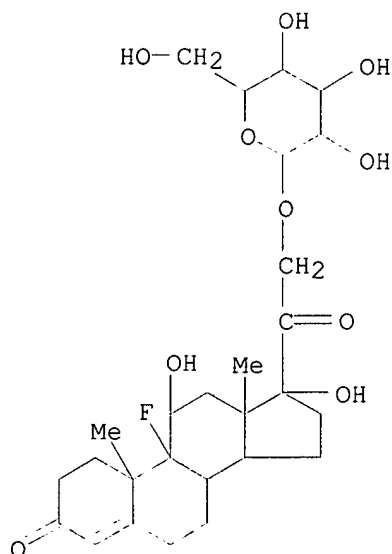
RN 92901-25-2 HCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)



RN 92901-26-3 HCAPLUS

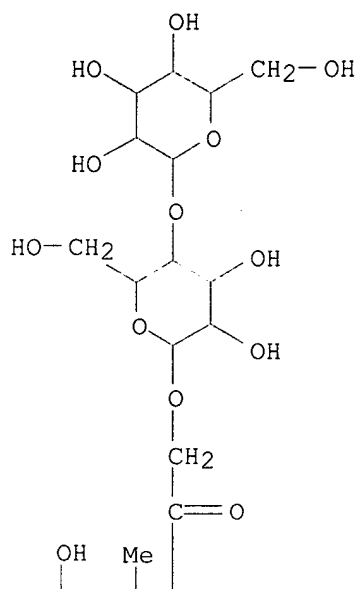
CN Pregn-4-ene-3,20-dione, 9-fluoro-21-(.beta.-D-galactopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)



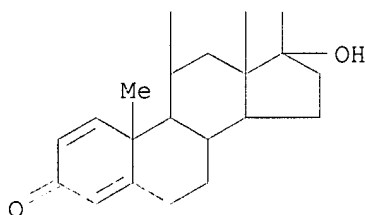
RN 92901-27-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[(4-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L103 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1984:73892 HCAPLUS
 DN 100:73892
 TI A colon-specific drug-delivery system based on drug glycosides and the
 glycosidases of colonic bacteria
 AU Friend, David R.; Chang, George W.
 CS Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA
 SO Journal of Medicinal Chemistry (1984), 27(3), 261-6
 CODEN: JMCMAR; ISSN: 0022-2623
 DT Journal
 LA English
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 2, 33
 GI For diagram(s), see printed CA Issue.
 AB The prodrugs 9.alpha.-fluoro-11.beta.,17.alpha.-dihydroxy-16.alpha.-methyl-
 3,20-dioxopregna-1,4-dien-21-yl .beta.-D-glucopyranoside (I) [88158-43-4]
 and 11.beta.,17.alpha.-dihydroxy-3,20-dioxopregna-1,4-
 dien-21-yl .beta.-D-glucopyranoside (II) [88158-44-5] which may
 be useful in treating **inflammatory** bowel disease were prepd. by
 coupling the appropriate steroid with 2,3,4,7-tetra-O-acetyl-1-bromo-

.alpha.-D-glucopyranose [572-09-8] followed by removal of the Ac protecting groups on the sugar residues from the steroid glucosides with 0.01N NaOH. I and II administered to rats intragastrically reached the rat lower intestine in 4-5 h, where they were rapidly hydrolyzed by the glycosidases of colon bacteria, releasing the free steroids. Nearly 60% of an oral dose of I reached the cecum, whereas <15% of II reached the cecum. The free steroids administered orally, were absorbed exclusively from the small intestine, <1% of either reached the cecum.

ST steroid glucoside prepn prodrug; colon drug delivery system

IT Intestine, metabolism

(colon, dexamethasone and prednisolone glucosides absorption by, delivery system in relation to)

IT Microorganism

(intestinal, steroid glucosides hydrolysis by, drug delivery system in relation to)

IT 50-02-2 50-24-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(coupling of, with bromotetraacetylglucopyranose, in prodrug prepn.)

IT 572-09-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(coupling of, with dexamethasone or prednisolone, in prodrugs prepn.)

IT 88158-45-6P 88179-95-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and hydrolysis of)

IT 88158-43-4P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as dexamethasone prodrug, in colon-specific delivery system)

IT 88158-44-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as prednisolone prodrug, in colon-specific delivery system)

IT 88158-45-6P 88179-95-7P

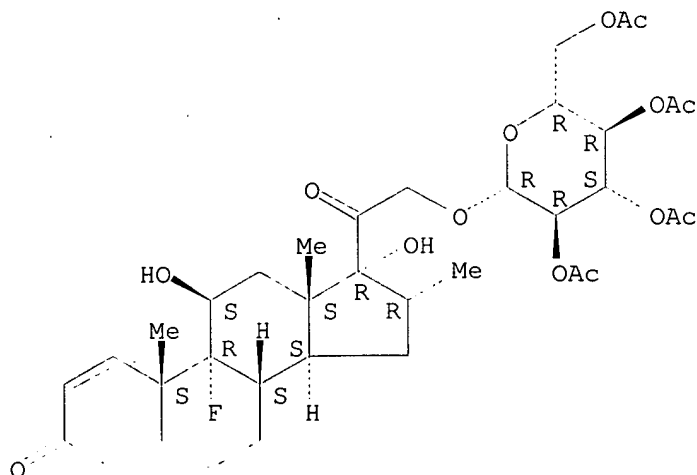
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and hydrolysis of)

RN 88158-45-6 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

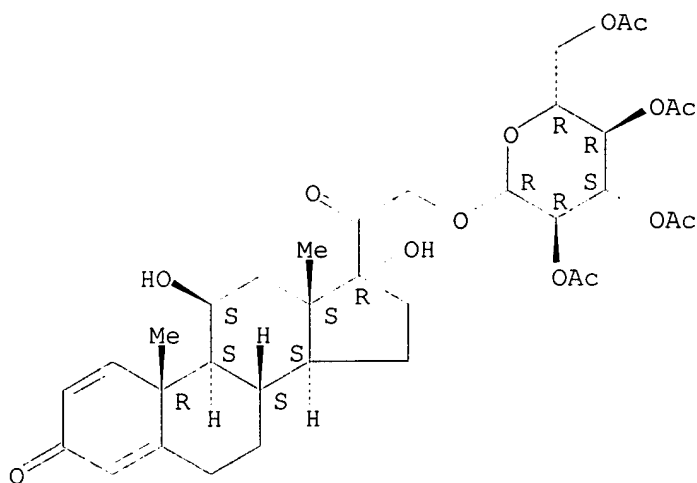
Absolute stereochemistry.



RN 88179-95-7 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(2,3,4,6-tetra-O-acetyl-.beta.-D-glucopyranosyl)oxy]-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



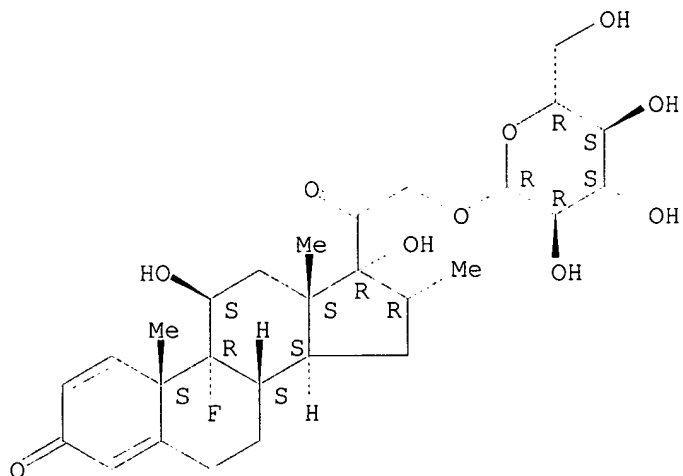
IT 88158-43-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as dexamethasone prodrug, in colon-specific delivery system)

RN 88158-43-4 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-16-methyl-, (11.beta.,16.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



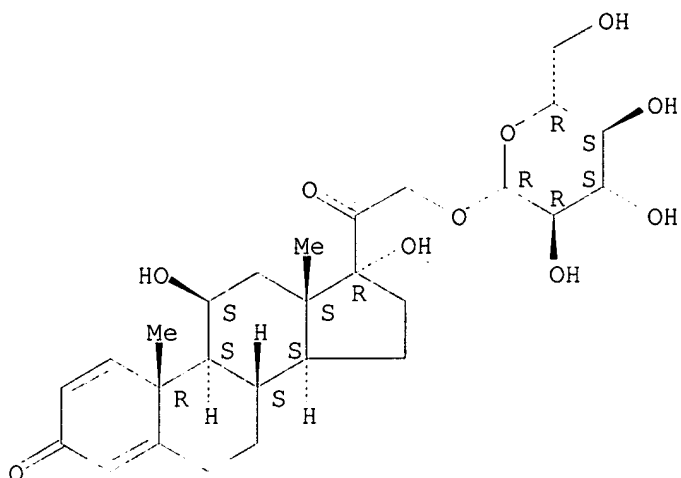
IT 88158-44-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as prednisolone prodrug, in colon-specific delivery system)

RN 88158-44-5 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranosyloxy)-11,17-dihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L103 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1970:21929 HCAPLUS

DN 72:21929

TI Steroidal 2'-acetamido-2'-deoxy-glucosidal **antiinflammatory** compounds

IN Sarett, Lewis H.; Strachan, Robert G.; Hirschmann, Ralph F.

PA Merck and Co., Inc.

SO U.S., 26 pp. Continuation-in-part of U.S. 3325474

CODEN: USXXAM

DT Patent

LA English

IC A61K; C07C

NCL 260210000

CC 33 (Carbohydrates)

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|--------------|
| PI | US 3427300 | A | 19690211 | US 1965-507522 | 19651112 <-- |
| AB | <p>A mixt. of 4.5 g. 11,17,21-trihydroxy-1,4-pregnadiene-3,20-dione in 25 ml dry HCONMe₂ contg. 17.6 g Hg(CN)₂ was dild. with 25 ml xylene, 13.0 g 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-.alpha.-O-glucopyranosyl chloride in 100 ml of 1:1 HCONMe₂-xylene was added dropwise over 3 hrs under n at 130-5.degree., the mixt. was kept at 130-5.degree. for 1.75 hrs, cooled, dild. with 500 ml CHCl₃, and worked up to yield 11,17-dihydroxy-3,20-dioxo-1,4-pregnadien-21-yl 2-acetamido-2-deoxy-.beta.-D-glucoside (I). A soln. of 27 millimoles I in 140 ml pyridine was cooled in an ice bath, 160 millimoles acetylsalicyloyl Cl was added in portions with stirring, t he mixt. was stirred at room temp. 10 hrs and worked up to yield 11,17-dihydroxy-3,20-dioxo-1,4-pregnadien-21-yl 2-acetamido-3,4,6-tri-O-(o-acetoxybenzoyl)-2-deoxy-.beta.-D-glucoside. Also prepd. were 9.alpha.-fluoro-11.beta.,17.alpha.,21-trihydroxy-3,20-dioxo-1,4-pregnadien-16.alpha.-yl 2-acetamido-2-deoxy-.beta.-D-glucoside; 11,17-dihydroxy-3,20-dioxo-1,4-pregnadien-21-yl 2-deoxy-2-trifluoroacetamido-.beta.-D-glucoside; 11,17-dihydroxy-3,20-dioxo-1,4-pregnadien-21-yl 2-amino-2-deoxy-.beta.-D-glucoside; 11.beta.-hydroxy-2-hydroxymethylene-17.alpha.,20,20,21-bismethylenedioxy-6,16.alpha.-dimethyl-4,6-pregnadien-3-one, m. 200-4.degree.; 17.alpha.,20,20,21-bis(methylenedioxy)-6,16.alpha.-dimethyl-2'-phenyl-[3,2-c]pyrazole-4,6-pregnadien-11.beta.-ol, m. 258-62.degree.; 11.beta.,17.alpha.,-21-trihydroxy-6,16.alpha.-dimethyl-2'-phenyl[3,2-c]pyrazolo-4,6-pregnadien-20-one and the 21-acetate m. 225-6.degree.. The resp. galactosides were also prepd.</p> | | | | |
| ST | steroidal glucosidyl antiinflammatorys ; glucosidyl steroidal | | | | |

antiinflammatorys; antiinflammatorys steroidal
glucosidyl

IT Steroids, preparation

RL: PREP (Preparation)

(2-acetamido-2-deoxyglycosides, inflammation-inhibiting
substances)

IT Glycosides

RL: RCT (Reactant)

(steroidal 2-acetamido-2-deoxy-, inflammation-inhibiting
substances)

IT 6736-63-6P 6736-65-8P 6736-66-9P 6736-67-0P 15466-03-2P

26783-53-9P 26783-54-0P 26783-55-1P 26783-58-4P

26783-59-5P 26783-60-8P 26783-61-9P 26783-62-0P 26783-63-1P

26783-64-2P 26783-65-3P 26783-66-4P 26783-67-5P 26783-68-6P

26884-47-9P 26884-48-0P 26884-49-1P 26940-50-1P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

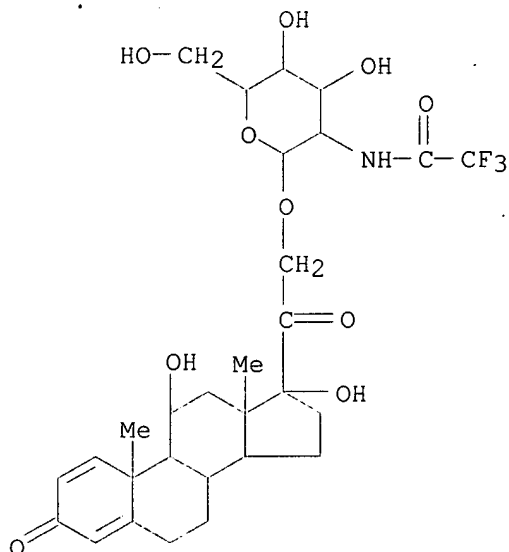
IT 26783-53-9P 26783-54-0P 26884-47-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

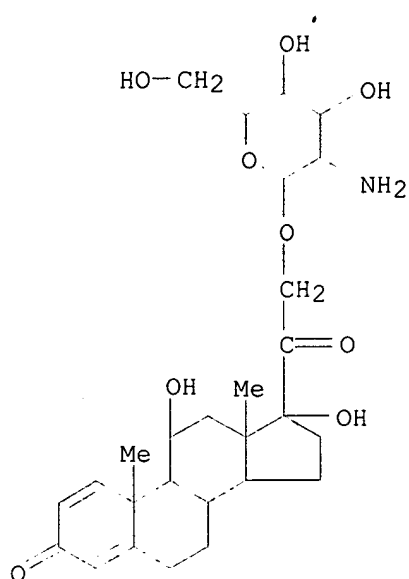
RN 26783-53-9 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[[2-deoxy-2-(2,2,2-trifluoroacetamido)-
.beta.-D-glucopyranosyl]oxy]-11,17-dihydroxy- (8CI) (CA INDEX NAME)

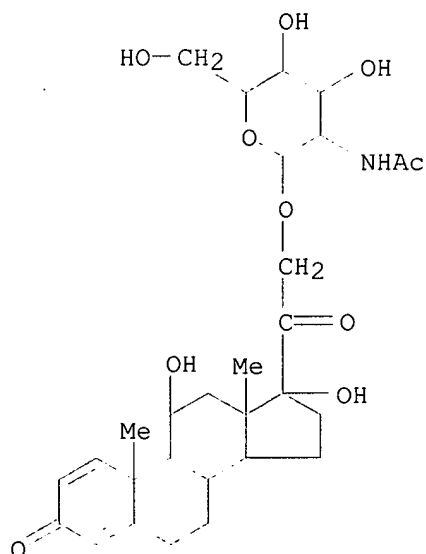


RN 26783-54-0 HCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[(2-amino-2-deoxy-.beta.-D-
glucopyranosyl)oxy]-11,17-dihydroxy- (8CI) (CA INDEX NAME)



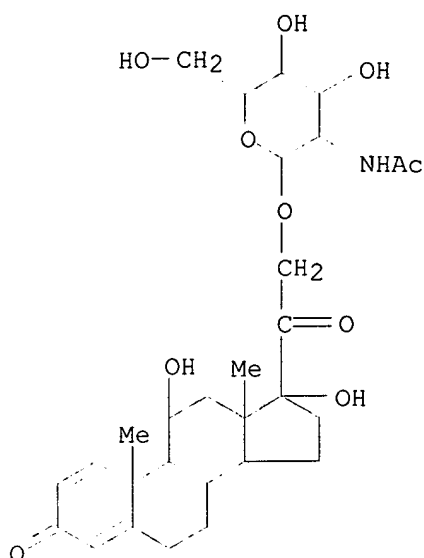
RN 26884-47-9 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 21-[(2-acetamido-2-deoxy-.beta.-D-glucopyranosyl)oxy]-11,17-dihydroxy- (8CI) (CA INDEX NAME)



L103 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1967:95370 HCAPLUS
 DN 66:95370
 TI 2-N-Acylamido-2-deoxyglucosides of steroids
 IN Sarett, Lewis H.; Strachan, Robert G.; Hirschmann, Ralph F.
 PA Merck and Co., Inc.
 SO Fr., 5 pp.
 CODEN: FRXXAK
 DT Patent
 LA French
 IC A61K; C07C
 CC 33 (Carbohydrates)

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|------|
| PI | FR 3627 | | 19651122 | | <-- |
| PRAI | US | | 19630218 | <-- | |
| AB | <p>2-Acetamido-2-deoxy-D-glucose (I) was prepd. from 2-amino-2-deoxy-D-glucose-HCl (yield 70%, m. 202-4.degree.) and converted to 2-acetamido tri-O-acetyl-2-deoxy-D-glucopyranosyl chloride (II) (26.8 g. from 25 g. I). To a soln. of 4.5 g. pregna-1,4-diene-11.beta.,17.alpha.,21-triol-3,20-dione in 25 ml. HCONMe2 contg. 17.6 g. Hg(CN)2 and 25 ml. abs. xylene was added dropwise during 3 hrs. (with stirring and under N) a soln. of 13 g. II in 100 ml. 1:1 HCONMe2-xylene at 130-5.degree. (oil bath), the mixt. held 1.75 hrs. at this temp., cooled, dild. with 500 ml. CHCl3, and washed with H2O (total 500 ml.), the aq. phase reextd. with CHCl3, the org. phase dried and evapd., the residue dissolved in (ClCH2)2, the solvent evapd., and the remainder dried in vacuo, taken up in CHCl3, and chromatographed on acid-washed Al2O3. Elution with CHCl3-MeOH (up to 95% MeOH) gave pregna-1,4-diene-11.beta.,17.alpha.-diol-3,20-dione-21-yl tri-O-acetyl-D-2-acetamido-2-deoxy-.beta.-D-glucopyranoside (III). A soln. of 1.055 g. III in 120 ml. MeOH treated under N with the calcd. amt. of MeONa (10 min. at room temp.), neutralized with AcOH, filtered, dild. with 6.5 ml. H2O, and centrifuged, and the supernatant cooled gave pregna-1,4-diene-11.beta.,17.alpha.-diol-3,20-dione-21-yl D-2-acetamido-2-deoxy-.beta.-D-glucopyranoside. Similarly, 9.alpha.-fluoropregna-1,4-diene-11.beta.,16.alpha.,17.alpha.,21-tetrol-3,20-dione 21-monoacetate was converted to 9.alpha.-fluoropregna-1,4-diene-11.beta.,17.alpha.,21-triol-3,20-dione-16.alpha.-yl D-2-acetamido-2-deoxy-.beta.-D-glucopyranoside. The new compds. are antiinflammatory agents, but have no side effects.</p> | | | | |
| IT | Steroids, preparation | | | | |
| | RL: PREP (Preparation) | | | | |
| | (2-acetamido-2-deoxy-.beta.-D-glucopyranosides) | | | | |
| IT | 3024-64-4P 15466-03-2P | | | | |
| | RL: SPN (Synthetic preparation); PREP (Preparation) | | | | |
| | (prepn. of) | | | | |
| IT | 3024-64-4P | | | | |
| | RL: SPN (Synthetic preparation); PREP (Preparation) | | | | |
| | (prepn. of) | | | | |
| RN | 3024-64-4 HCAPLUS | | | | |
| CN | Pregna-1,4-diene-3,20-dione, 21-[(2-acetamido-2-deoxy-.beta.-D-glucopyranosyl)oxy]-11.beta.,17-dihydroxy- (7CI, 8CI) (CA INDEX NAME) | | | | |



L103 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1965:480944 HCAPLUS

DN 63:80944

OREF 63:14968e-h,14969a

TI Steroid D-galactouronides

IN Sarett, Lewis H.; Strachan, Robert G.; Hirschmann, Ralph F.

PA Merck & Co., Inc.

SO 91 pp.

DT Patent

LA Unavailable

CC 43 (Carbohydrates)

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|------------|------|----------|-----------------|------|
| PI | BE 643983 | | 19640818 | BE | <-- |
| | GB 1047542 | | | GB | |
| | US 3206359 | | 1965 | US | <-- |
| | US 3240777 | | 1966 | US | <-- |
| PRAI | US | | 19630218 | <-- | |

GI For diagram(s), see printed CA Issue.

AB Compds. of the general formula I, where Z is a steroid residue R is an alkyl group, Ba, or Na, and Y is H or an acyl group, are prep'd. and can be used as **antiinflammatory** agents. Thus, a mixt. of .apprx.0.015 mole prednisolone and 0.03 mole Ag₂CO₃ in 350 ml. C₆H₆ is treated with 0.02 mole methyl (tri-O-acetyl-.alpha.-D-galactopyranosyl bromide)uronate to give methyl (11.beta.,17.alpha.-dihydroxy-1,4-pregnadiene-3,20-dione-21-yl tri-O-acetyl-.beta.-D-galactopyranoside)uronate (II), .lambda.max 243 m.mu. (E 197). Similarly prep'd. is methyl (16.alpha.-methyl-11.beta.,17.alpha.-dihydroxy-4-pregnene-3-,20-dione-21-yl tri-O-acetyl-.beta.-D-galactopyranoside)uronate, .lambda.max. 240 m.mu. (E .apprx.200). A soln. of 0.005 mole II in 70 ml. MeOH is treated with 20 ml. N NaOMe(MeOH), the mixt. is agitated 30 min. under N, and 250 ml. 0.1N Ba(OH)₂ is added to give 11.beta.,17.alpha.,21-trihydroxy-1,4-pregnadiene-3,20-dione barium 21-D-galactouronide (III). A soln. of 0.001 mole III in H₂O is treated with 30 g. Amberlite IRC-50 (Na form) to give 11.beta.,17.alpha.,21-trihydroxy-1,4-pregnadiene-3,20-dione sodium 21-D-galactouronide, .lambda.max. 246 m.mu. (E .apprx.167). Also prep'd. are 3.alpha.-acetoxy-16.alpha.-methylpregnane-11,20-dione, 3.alpha.,20-diacetoxy-16.alpha.-methyl-17(20)-pregnen-11-one,

17.alpha.,20-epoxy-3.alpha.,20- epoxy-3.alpha.,20-diacetoxy-16.alpha.-methyl-pregnane-11-one, 3.alpha.,17.alpha.-dihydroxy-16.alpha.-methyl-pregnane-11,20-dione, 21-bromo-3.alpha.,17.alpha.-dihydroxy-16.alpha.-methyl-pregnane-11,20-dione, 3.alpha.,17.alpha.,21-trihydroxy-16.alpha.-methyl-pregnane-11,20-dione, 17.alpha.,21-dihydroxy-16.alpha.-methylpregnane-3,11,20-trione 21-acetate, 4-bromo-17.alpha.,21-dihydroxy-16.alpha.-methylpregnane-3,11,20-trione, 3,20-bissemicarbazido-17.alpha.,21-dihydroxy 16.alpha.-methyl-4-pregnene-3,11,20-trione, 3,20-bissemicarbazido-11.beta.,17.alpha.,21-trihydroxy-16.alpha.-methyl-4-pregnene-3,20-dione, 11.beta.,17.alpha.,21-trihydroxy-16.alpha.-methyl-4-pregnene-3,20-dione, 6,16.alpha.-dimethyl-11.beta.,17.alpha.,21 - trihydroxy-2'-phenyl[3,2-c]pyrazolo-4,6-pregnadien-20-one (IV), IV 21-acetate (m. 225-6.degree.), 6,16.alpha.-dimethyl- 11.beta.,17.alpha.,21 - trihydroxy[3,2-c]pyrazolo-4,6-pregnadiene-20-one.

IT Steroids

(D-galactopyranuronosides)

- IT 5.beta.-Pregn-15-ene-11,20-dione, 3.alpha.,17-dihydroxy-16-methyl-, mixt. with 3.alpha.,17-dihydroxy-16-methylene-5.beta.-pregnane-11,20-dione
5.beta.-Pregnane-11,20-dione, 17,16.alpha.-(azomethylene)-3.alpha.-hydroxy-, acetate
5.beta.-Pregnane-11,20-dione, 3.alpha.,17-dihydroxy-16-methylene-, mixt. with 3.alpha.,17-dihydroxy-16-methyl-5.beta.-pregn-15-ene-11,20-dione
Dispiro[cyclopenta[7,8]phenanthro[2,3-c]pyrazole-1(2H),4'-[1,3]dioxolane-5',4'-[1,3]dioxolan]-11-ol, 3,3a,3b,7,10,10a,10b,11,12a-decahydro-2,5,10a,12a-tetramethyl-7-phenyl-
Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D-
Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-
Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-6,16.alpha.-dimethyl-3,20-di-oxopregna-4,6-dien-21-yl, sodium salt, .beta.-D-
Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-6.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D-
Galactopyranosiduronic acid, 6.alpha.-fluoro-11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D-
Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,17-dihydroxy-16.alpha.-methyl-3,-20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D-
Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,17-dihydroxy-16.beta.-methyl-3,-20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D-
Galactopyranosiduronic acid, [(1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1,11-dihydroxy-2,5,10a,12a-tetramethylcyclopenta[7,8]phenanthro[2,3-c]pyrazol-1-yl)carbonyl]methyl, methyl ester, 2,3,4-triacetate, .beta.-D-
Ketone, 1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1,11-dihydroxy-2,5,10a,12a-tetramethyl-7-phenylcyclopenta[7,8]phenanthro[2,3-c]pyrazol-1-yl hydroxymethyl, acetate (ester)
Naphth[2',1':4,5]indeno[1,2-c]pyrazol-5(2H)-one, 6b-acetyl-1,3,4,4a,4b,6,6a,6b,9,9a,10,10a,10b,11,12,12a-hexadecahydro-2-hydroxy-4a,6a-dimethyl-, acetate (ester)
Pregn-4-ene-3,20-dione, 21-(.beta.-D-glucopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, 2',3',4'-triacetate
Pregn-4-ene-3,20-dione, 21-(.beta.-D-glucopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, sodium salt
Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-, sodium salt
Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, sodium salt
Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-6.alpha.-methyl-, sodium salt
Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranuronosyloxy)-11.beta.,17-dihydroxy-, methyl ester, 2',3',4'-triacetate

Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,16.alpha.,17-trihydroxy-, cyclic 16,17-acetal with acetone
 Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, sodium salt
 Pregna-4,6-dieno[3,2-c]pyrazol-11.beta.-ol, 6,16.alpha.-dimethyl-17,20:20,21-bis(methylenedioxy)-2'-phenyl-
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 11.beta.,17,21-trihydroxy-6,16.alpha.-dimethyl-
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 11.beta.,17,21-trihydroxy-6,16.alpha.-dimethyl-2'-phenyl-
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 11.beta.,17,21-trihydroxy-6,16.alpha.-dimethyl-2'-phenyl-, 21-acetate
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-6,16.alpha.-dimethyl-, methyl ester, 2',3',4'-triacetate
 IT 802-82-4, 5.beta.-Pregnane-11,20-dione, 16.alpha.,17-epoxy-3.alpha.-hydroxy-16-methyl- 803-09-8, 5.beta.-Pregnane-11,20-dione, 3.alpha.,17-dihydroxy-16.beta.-methyl- 978-83-6, 5.beta.-Pregnane-11,20-dione, 3.alpha.,17-dihydroxy-16.alpha.-methyl- 983-48-2, 5.beta.-Pregn-16-ene-11,20-dione, 3.alpha.-hydroxy-16-methyl-, acetate 1058-04-4, Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-16.alpha.-methyl-, 21-acetate 1247-42-3, Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-16.beta.-methyl- 1253-36-7, 5.beta.-Pregnane-3,11,20-trione, 17,21-dihydroxy-16.beta.-methyl-, 21-acetate 1255-27-2, 5.beta.-Pregnane-3,11,20-trione, 4-bromo-17,21-dihydroxy-16.beta.-methyl-, 21-acetate 4107-07-7, 5.beta.-Pregnane-3,11,20-trione, 2,4-dibromo-17,21-dihydroxy-16.beta.-methyl-, 21-acetate **4107-13-5**, Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,16.alpha.,17-trihydroxy-3,20-dioxopregna-1,4-dien-21-yl, .beta.-D- **4107-13-5**, Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,16.alpha.,17-trihydroxy- 4107-14-6, Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,16.alpha.,17-trihydroxy-3,20-dioxopregna-1,4-dien-21-yl, cyclic 16,17-acetal with acetone, .beta.-D- **4157-49-7**, Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.beta.-methyl-, sodium salt **4157-50-0**, Pregna-1,4-diene-3,20-dione, 6.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-, sodium salt 4157-51-1, Pregna-4,6-diene-3,20-dione, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-6,16.alpha.-dimethyl- **4157-53-3**, Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, 2',3',4'-triacetate **4157-53-3**, Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,17-dihydroxy-16.alpha.-methyl-3,-20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D- 4183-48-6, 5.beta.-Pregnane-11,20-dione, 3.alpha.-hydroxy-16.alpha.-methyl-, acetate 4183-49-7, 5.beta.-Pregnane-11,20-dione, 21-bromo-3.alpha.,17-dihydroxy-16.alpha.-methyl- **4193-32-2**, Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D- **4206-90-0**, Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D- 4466-28-8, Ketone, 1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1,11-dihydroxy-2,5,10a,12a-tetramethylcyclopenta[7,8]phenanthro[2,3-c]pyrazol-1-yl hydroxymethyl 4906-84-7, Ketone, 1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1,11-dihydroxy-2,5,10a,12a-tetramethyl-7-phenylcyclopenta[7,8]phenanthro[2,3-c]pyrazol-1-yl hydroxymethyl 5059-58-5, Pregna-4,6-dien-3-one, 11.beta.-hydroxy-2-(hydroxymethylene)-6,16.alpha.-dimethyl-17,20:20,21-bis(methylenedioxy)- **5132-78-5**, Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, 2',3',4'-triacetate **5132-78-5**,

Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-34614-33-0, 5.beta.-Pregnane-3,11,20-trione, 4-bromo-17,21-dihydroxy-16.alpha.-methyl-, 21-acetate **107079-42-5**, Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, sodium salt, .beta.-D-

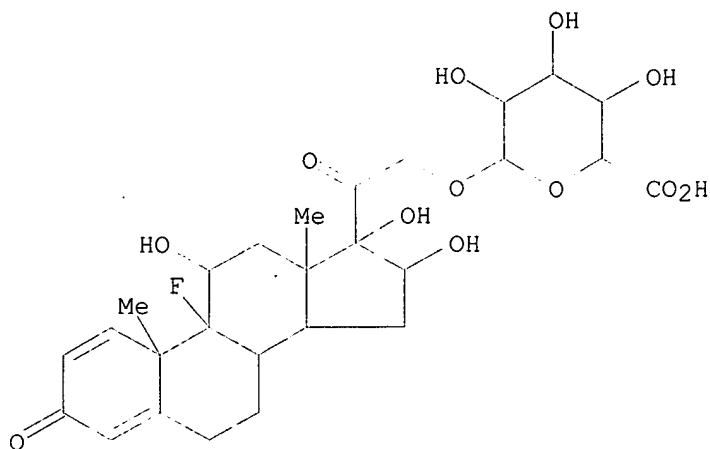
(prepn. of)

IT **4107-13-5**, Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,16.alpha.,17-trihydroxy-3,20-dioxopregna-1,4-dien-21-yl, .beta.-D- **4157-49-7**, Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.beta.-methyl-, sodium salt **4157-50-0**, Pregna-1,4-diene-3,20-dione, 6.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-, sodium salt **4157-53-3**, Pregna-1,4-diene-3,20-dione, 9.alpha.-fluoro-21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, 2',3',4'-triacetate **4193-32-2**, Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D- **4206-90-0**, Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D- **5132-78-5**, Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-galactopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, 2',3',4'-triacetate **107079-42-5**, Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, sodium salt, .beta.-D-

(prepn. of)

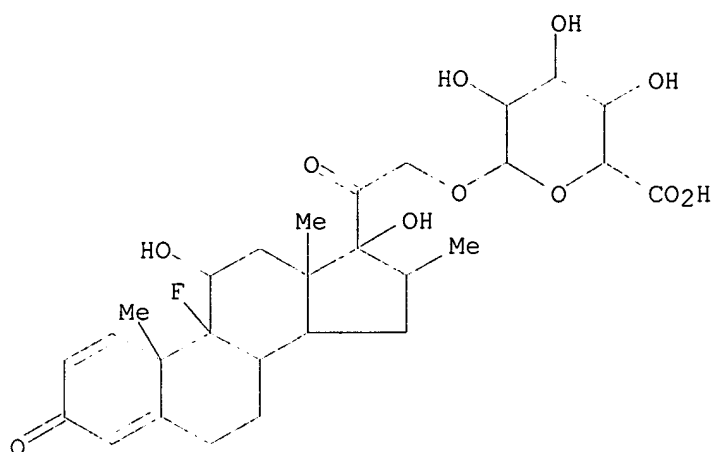
RN 4107-13-5 HCAPLUS

CN Galactopyranosiduronic acid, 9.alpha.-fluoro-11.beta.,16.alpha.,17-trihydroxy-3,20-dioxopregna-1,4-dien-21-yl, .beta.-D- (8CI) (CA INDEX NAME)



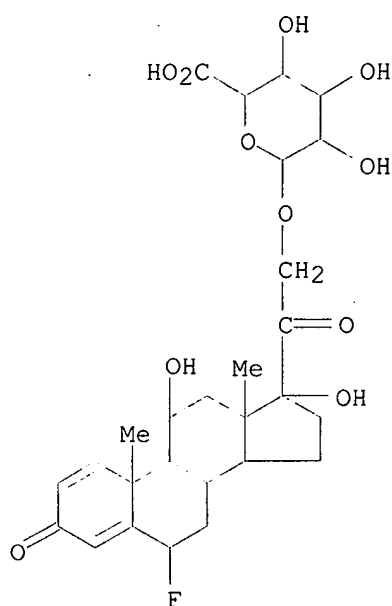
RN 4157-49-7 HCAPLUS

CN .beta.-D-Galactopyranosiduronic acid, (11.beta.,16.beta.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, monosodium salt (9CI) (CA INDEX NAME)



● Na

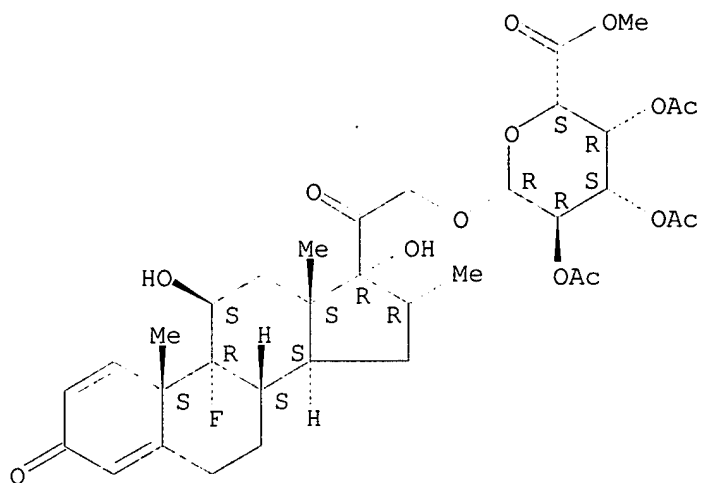
RN 4157-50-0 HCAPLUS
 CN .beta.-D-Galactopyranosiduronic acid, (6.alpha.,11.beta.)-6-fluoro-11,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, monosodium salt (9CI) (CA INDEX NAME)



● Na

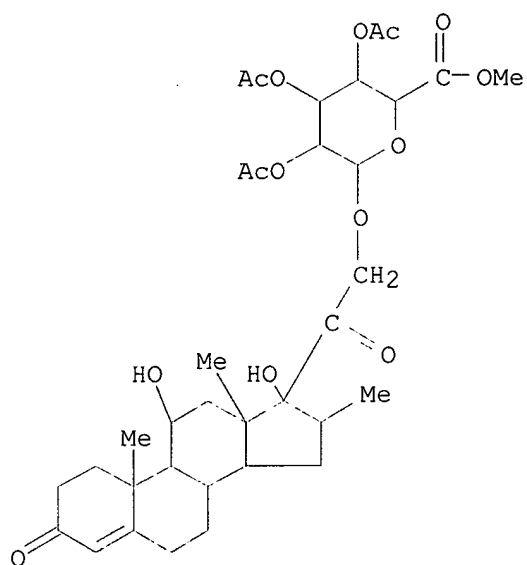
RN 4157-53-3 HCAPLUS
 CN .beta.-D-Galactopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



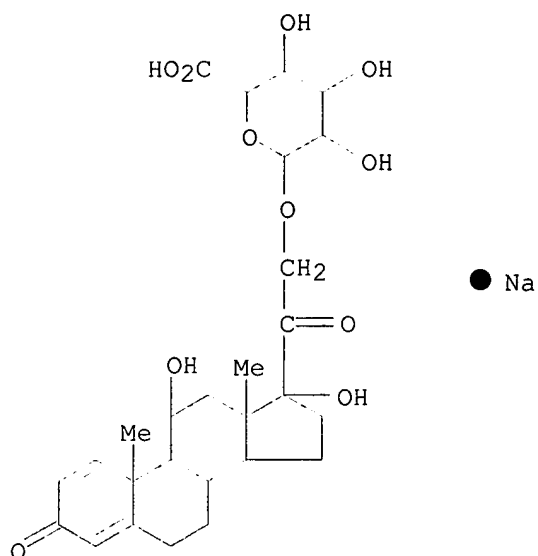
RN 4193-32-2 HCAPLUS

CN Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D- (8CI)
(CA INDEX NAME)

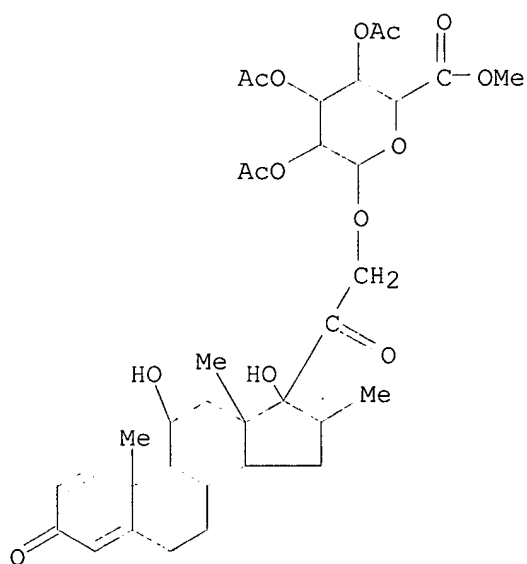


RN 4206-90-0 HCAPLUS

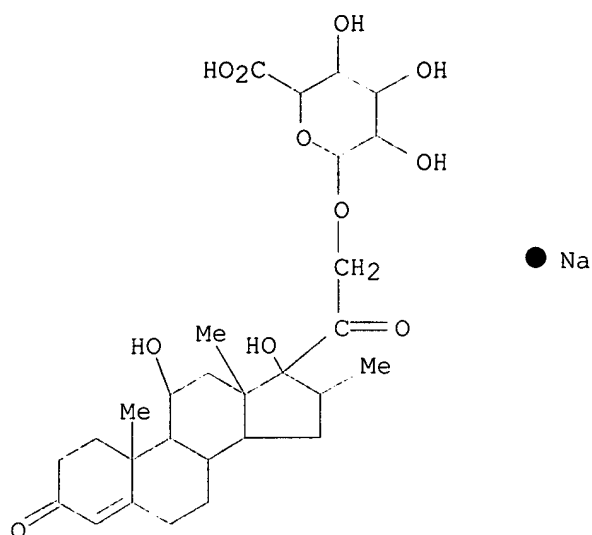
CN Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, sodium salt, .beta.-D- (8CI) (CA INDEX NAME)



RN 5132-78-5 HCAPLUS
 CN Galactopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-(8CI) (CA INDEX NAME)



RN 107079-42-5 HCAPLUS
 CN Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-4-en-21-yl, sodium salt, .beta.-D- (7CI) (CA INDEX NAME)



L103 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1965:3285 HCAPLUS

DN 62:3285

OREF 62:626h, 627a

TI Approach to an improved **antiinflammatory** steroid. Synthesis of 11.β., 17-dihydroxy-3, 20-dioxo-1, 4-pregnadien-21-yl 2-acetamido-2-deoxy-β.-D-glucopyranoside

AU Hirschmann, Ralph; Strachan, Robert G.; Buchschacher, P.; Sarett, L. H.; Steelman, S. L.; Silber, R.

CS Merck & Co. Inc., Rahway, NJ

SO J. Am. Chem. Soc. (1964), 86(18), 3903-4

CODEN: JACSAT; ISSN: 0002-7863

DT Journal

LA English

CC 43 (Carbohydrates)

AB Prednisolone (I) condensed with 2-acetamido-3, 4, 6-tri-O-acetyl-2-deoxy-α.-D-glucopyranosyl chloride yielded 11.β., 17-dihydroxy-3, 20-dioxo-1, 4-pregnadien-21-yl 2-acetamido-3, 4, 6-tri-O-acetyl-2-deoxy-β.-D-glucopyranoside, which methanolized gave the title compd. (II). Incubation of II with β.-N-acetylglucosaminidase gave the theoretical amt. of I; the hydrolysis was inhibited by 2-acetamido-2-deoxy-D-gluconolactone. II showed **antiinflammatory** effects.

IT **Inflammation**

Inflammation

(inhibitors of, 21-[(2-acetamido-2-deoxy-β.-D-glucopyranosyl)oxy]-11.β., 17-dihydroxypregna-1, 4-diene-3, 20-dione as)

IT Spectra, visible and ultraviolet

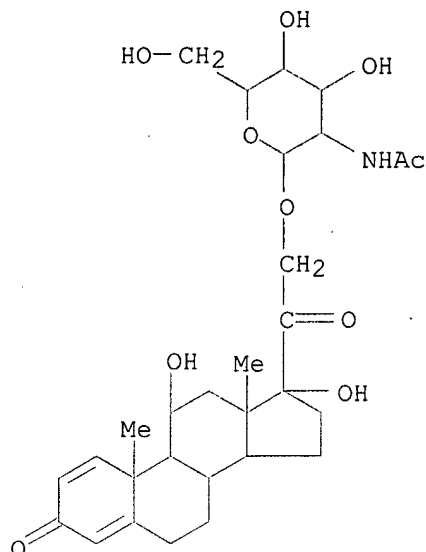
(of 21-[(2-acetamido-2-deoxy-β.-D-glucopyranosyl)oxy]-11.β., 17-dihydroxypregna-1, 4-diene-3, 20-dione and its triacetate)

IT Glucopyranoside, 11.β., 17-dihydroxy-3, 20-dioxopregna-1, 4-dien-21-yl 2-acetamido-2-deoxy-, triacetate

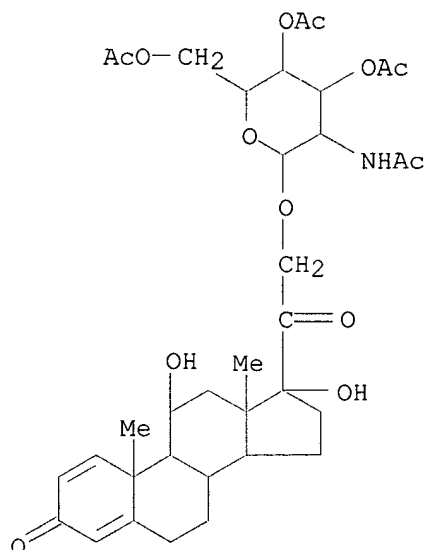
IT **3024-64-4**, Pregna-1, 4-diene-3, 20-dione, 21-[(2-acetamido-2-deoxy-β.-D-glucopyranosyl)oxy]-11.β., 17-dihydroxy- **3056-39-1**, Pregna-1, 4-diene-3, 20-dione, 21-[(2-acetamido-2-deoxy-β.-D-glucopyranosyl)oxy]-11.β., 17-dihydroxy-, 3', 4', 6'-triacetate (prepn. of)

IT **3024-64-4**, Pregna-1, 4-diene-3, 20-dione, 21-[(2-acetamido-2-deoxy-β.-D-glucopyranosyl)oxy]-11.β., 17-dihydroxy- **3056-39-1**, Pregna-1, 4-diene-3, 20-dione, 21-[(2-acetamido-2-deoxy-β.-D-glucopyranosyl)oxy]-11.β., 17-dihydroxy-, 3', 4', 6'-triacetate

(prepn. of)
 RN 3024-64-4 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 21-[(2-acetamido-2-deoxy-.beta.-D-glucopyranosyl)oxy]-11.beta.,17-dihydroxy- (7CI, 8CI) (CA INDEX NAME)



RN 3056-39-1 HCAPLUS
 CN Pregna-1,4-diene-3,20-dione, 21-[(2-acetamido-2-deoxy-.beta.-D-glucopyranosyl)oxy]-11.beta.,17-dihydroxy-, 3',4',6'-triacetate (7CI, 8CI) (CA INDEX NAME)



L103 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1964:91214 HCAPLUS

DN 60:91214

OREF 60:15974e-g

TI **Antiinflammatory** steroid compositions

IN Sarett, Lewis H.; Strachan, Robert G.; Hirschmann, Ralph

PA Merck & Co., Inc.
 SO 25 pp.
 DT Patent
 LA Unavailable
 CC 43 (Carbohydrates)

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|------------|------|----------|-----------------|------|
| PI | BE 623144 | | 19630403 | BE | <-- |
| | FR M2271 | | | FR | |
| | GB 1015396 | | | GB | |
| | US 3185682 | | 1965 | US | <-- |
| PRAI | US | | 19611004 | <-- | |

AB The 21-glucuronides of 11,17-dihydroxy-20-oxo-21-hydroxy ring A-unsatd. steroids of the pregnane series are conveniently prepd. by treating pregnane, at an elevated temp., with lower alkyl tri-O-acyl-.alpha.-D-bromoglucuronates in an inert solvent such as C₆H₆ in the presence of Ag₂CO₃. Treatment of the resulting 21-(tri-O-acyl-.alpha.-D-glucuronide) esters with an aq.-alc. soln. of an alkoxide, Ba(OH)₂, or with ion exchange resin (alkali metal form), yields the corresponding salt of the 21-glucuronide of the steroid. Ultraviolet absorption spectra were as follows: 11.beta.,17.alpha.-dihydroxy-1,4-pregnadiene-3,20-dion-21-yl tri-O-acetyl-.beta.-D-glucuronide Me ester, .lambda. 243 m.mu. (.vepsiln. 197); 16.alpha.-methyl-11.beta., 17.alpha.-dihydroxy-4-pregnene-3,20-dion-21-yl tri-O-acetyl-.beta.-D-glucuronide Me ester, .lambda. 240 m.mu. (.vepsiln. .apprx.200); 11.beta., 17.alpha.-dihydroxy-1,4-pregnadiene-3,20-dion-21-yl .beta.-D-glucuronide Na salt, .lambda.. 246 m.mu. (.vepsiln. 167).

IT Steroids

(inflammation inhibition by)

IT Inflammation

Inflammation

(inhibitors of, steroids as)

IT Glucopyranosiduronic acid, 9-fluoro-11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-

Glucopyranosiduronic acid, [(1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1.alpha.,11.beta.-dihydroxy-2.alpha.,5-dimethyl-cyclopenta[7,8]phenanthro[2,3-c]pyrazol-1-yl)carbonyl]methyl, methyl ester, 2,3,4-triacetate

Glucosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, sodium salt

Glucosiduronic acid, 11.beta.17-dihydroxy-6.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, sodium salt

Glucosiduronic acid, 6.alpha.-fluoro-11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, sodium salt

Glucosiduronic acid, 9-fluoro-11.beta.-hydroxy-16.alpha.,17-(isopropylidenedioxy)-3,20-dioxopregna-1,4-dien-21-yl

Glucosiduronic acid, [(1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1,11-dihydroxy-2,5-dimethylcyclopenta[7,8]phenanthro[2,3-c]-pyrazol-1-yl)carbonyl]methyl, sodium salt

Glucosiduronic acid, [(1,2,3,3a,3b,7,10,10a,10b,11,12,12a-dodecahydro-1.alpha.,11.beta.-dihydroxy-2.alpha.,5-dimethyl-7-phenylcyclopenta[7,8]phenanthro[2,3-c]pyrazol-1-yl)carbonyl]-methyl, sodium salt

Pregn-4-ene-3,20-dione, 21-(glucuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, sodium salt

Pregn-4-ene-3,20-dione, 21-(.beta.-D-glucopyranuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, 2',3',4'-triacetate

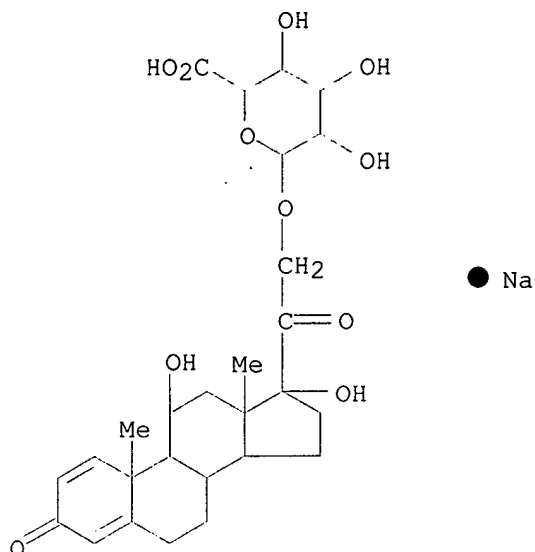
Pregna-1,4-diene-3,20-dione, 21-(glucuronosyloxy)-11.beta.,17-dihydroxy-, sodium salt

Pregna-1,4-diene-3,20-dione, 21-(glucuronosyloxy)-11.beta.,17-dihydroxy-16.alpha.-methyl-, sodium salt

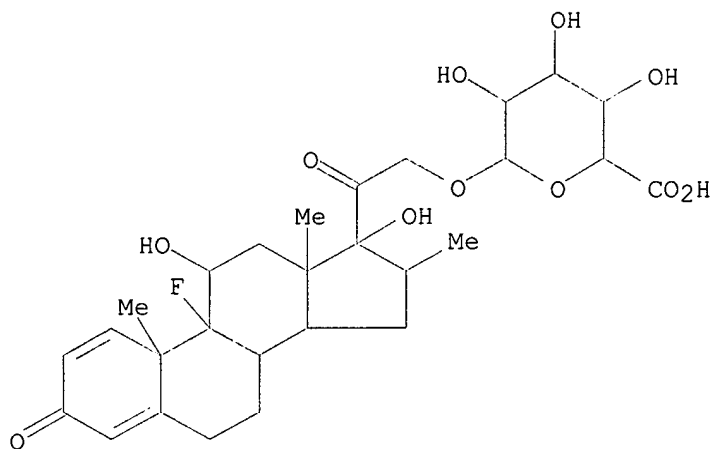
Pregna-1,4-diene-3,20-dione, 21-(glucuronosyloxy)-11.beta.,17-dihydroxy-

- 6.alpha.-methyl-, sodium salt
 Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranuronosyloxy)-
 11.beta.,17-dihydroxy-, methyl ester, 2',3',4'-triacetate
 Pregna-1,4-diene-3,20-dione, 21-(.beta.-D-glucopyranuronosyloxy)-
 11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester,
 2',3',4'-triacetate
 Pregna-1,4-diene-3,20-dione, 6.alpha.-fluoro-21-(glucuronosyloxy)-
 11.beta.,17-dihydroxy-, sodium salt
 Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(glucuronosyloxy)-
 11.beta.,16.alpha.,17-trihydroxy-, cyclic 16,17-acetal with acetone
 Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(glucuronosyloxy)-11.beta.,17-
 dihydroxy-16.alpha.-methyl-, sodium salt
 Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(glucuronosyloxy)-11.beta.,17-
 dihydroxy-16.beta.-methyl-, sodium salt
 Pregna-1,4-diene-3,20-dione, 9-fluoro-21-(.beta.-D-glucopyranuronosyloxy)-
 11.beta.,17-dihydroxy-16.alpha.-methyl-, methyl ester, triacetate
 Pregna-4,6-diene-3,20-dione, 21-(glucuronosyloxy)-11.beta.,17-dihydroxy-
 6,16.alpha.-dimethyl-, sodium salt
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 21-(glucosiduronosyloxy)-
 11.beta.,17.alpha.-dihydroxy-6,16.alpha.-dimethyl-, sodium salt
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 21-(glucosiduronosyloxy)-
 11.beta.,17.alpha.-dihydroxy-6,16.alpha.-dimethyl-2'-phenyl-, sodium
 salt
 Pregna-4,6-dieno[3,2-c]pyrazol-20-one, 21-(.beta.-D-glucopyranuronosyloxy)-
 11.beta.,17.alpha.-dihydroxy-6,16.alpha.-dimethyl-, methyl ester,
 triacetate
- IT Cyolopenta[7,8]phenanthro[2,3-c]pyrazole
 (steroid derivs.)
- IT 103365-98-6, Glucosiduronic acid, 11.beta.,17-dihydroxy-3,20-
 dioxopregna-1,4-dien-21-yl, sodium salt 105088-07-1,
 Glucosiduronic acid, 9-fluoro-11.beta.,17-dihydroxy-16.beta.-methyl-3,20-
 dioxopregna-1,4-dien-21-yl, sodium salt 105088-08-2,
 Glucosiduronic acid, 9-fluoro-11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-
 dioxopregna-1,4-dien-21-yl, sodium salt 105477-23-4,
 Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-
 dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-
 105477-24-5, Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-
 16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, methyl ester,
 2,3,4-triacetate, .beta.-D- 105560-80-3, Glucopyranosiduronic
 acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, methyl ester,
 2,3,4-triacetate, .beta.-D- 106819-74-3, Glucosiduronic acid,
 11.beta.,17-dihydroxy-6,16.alpha.-dimethyl-3,20-dioxopregna-4,6-dien-21-
 yl, sodium salt 107079-42-5, Glucosiduronic acid,
 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, sodium
 salt
 (prepn. of)
- IT 221-46-5, 1H-Naphth[2',1':4,5]indeno[1,2-d][1,3]dioxole
 (steroid derivs.)
- IT 103365-98-6, Glucosiduronic acid, 11.beta.,17-dihydroxy-3,20-
 dioxopregna-1,4-dien-21-yl, sodium salt 105088-07-1,
 Glucosiduronic acid, 9-fluoro-11.beta.,17-dihydroxy-16.beta.-methyl-3,20-
 dioxopregna-1,4-dien-21-yl, sodium salt 105088-08-2,
 Glucosiduronic acid, 9-fluoro-11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-
 dioxopregna-1,4-dien-21-yl, sodium salt 105477-23-4,
 Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-
 dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-
 105477-24-5, Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-
 16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, methyl ester,
 2,3,4-triacetate, .beta.-D- 105560-80-3, Glucopyranosiduronic
 acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, methyl ester,
 2,3,4-triacetate, .beta.-D- 107079-42-5, Glucosiduronic acid,
 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, sodium
 salt

(prepn. of)
 RN 103365-98-6 HCAPLUS
 CN Glucosiduronic acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, sodium salt (7CI) (CA INDEX NAME)



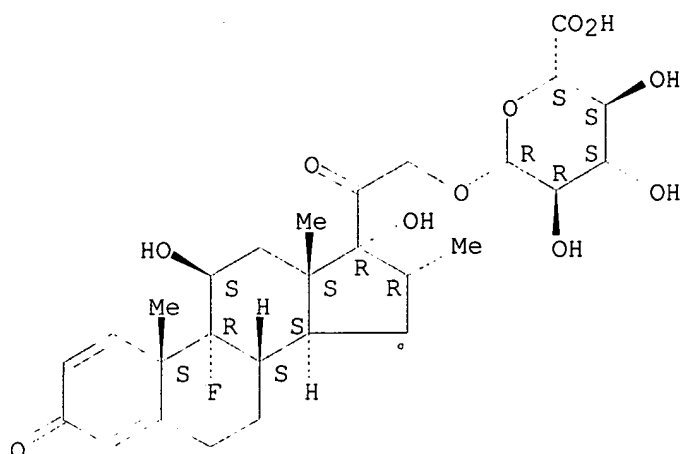
RN 105088-07-1 HCAPLUS
 CN Glucosiduronic acid, 9-fluoro-11.beta.,17-dihydroxy-16.beta.-methyl-3,20-dioxopregna-1,4-dien-21-yl, sodium salt (7CI) (CA INDEX NAME)



● Na

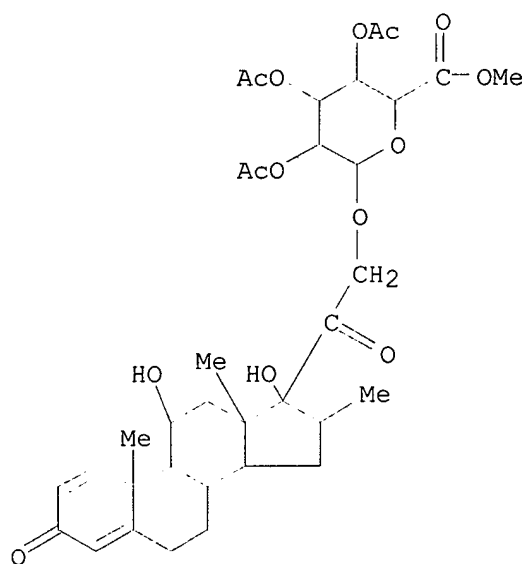
RN 105088-08-2 HCAPLUS
 CN .beta.-D-Glucopyranosiduronic acid, (11.beta.,16.alpha.)-9-fluoro-11,17-dihydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-yl, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

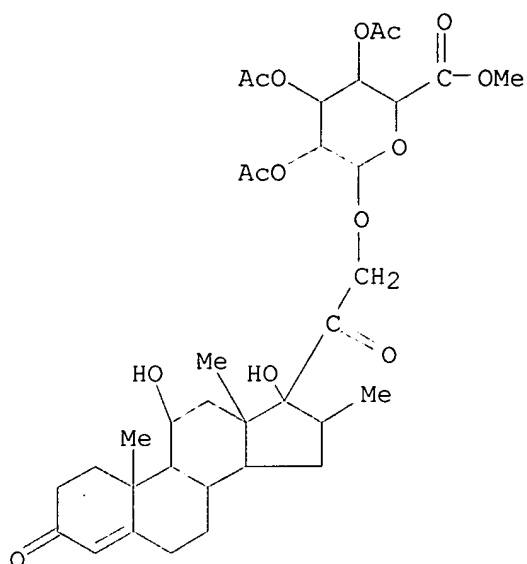


● Na

RN 105477-23-4 HCAPLUS
 CN Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D-(7CI) (CA INDEX NAME)

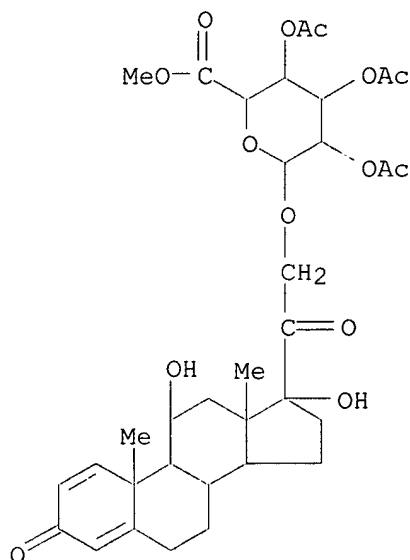


RN 105477-24-5 HCAPLUS
 CN Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D- (7CI) (CA INDEX NAME)



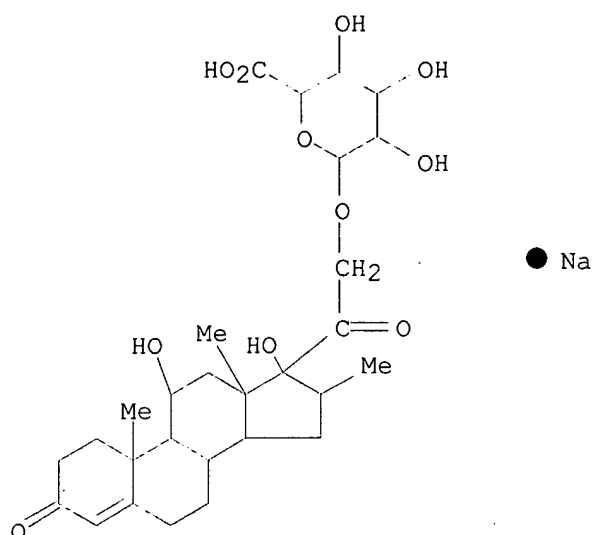
RN 105560-80-3 HCAPLUS

CN Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl, methyl ester, 2,3,4-triacetate, .beta.-D- (7CI) (CA INDEX NAME)



RN 107079-42-5 HCAPLUS

CN Glucopyranosiduronic acid, 11.beta.,17-dihydroxy-16.alpha.-methyl-3,20-dioxopregn-4-en-21-yl, sodium salt, .beta.-D- (7CI) (CA INDEX NAME)



L103 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 1963:469413 HCAPLUS

DN 59:69413

OREF 59:12912b-c

TI Steroid 21-O-glucosyluronamides

IN Nitta, Yoshihiro; Takamura, Keiichi; Shindo, Minoru

PA Chugai Pharmaceutical Co., Ltd.

SO 2 pp.

DT Patent

LA Unavailable

CC 43 (Carbohydrates)

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|-------------|------|----------|-----------------|--------------|
| PI | JP 38006774 | | 19630522 | JP | 19600506 <-- |

AB A mixt. of 2.2 g. Me pregn-4-ene-17.alpha.,21-diol-3,20-dione 21-O(2,3,4-tri-O-acetyl-D-glucosyl)uronate and 100 cc. NH3-satd MeOH at -5 to 0.degree. is kept overnight, the soln. concd. to 1/3 vol., kept overnight again, the resulting ppt. dissolved in 300 cc. MeOH, concd. to 1/3 vol., and treated with C to give 1.3 g. pregn-4-ene-17.alpha.,21-diol-3,20-dione 21-O-glucosyluronamide, m. 242.5-43.degree. (decompn.). Similarly prepd. are pregn-4-ene-17.alpha.,21-diol-3,11,20-trione 21-O-glucosyluronamide [m. 254-5.degree. (decompn.)], pregn-4-ene-11.beta.,17.alpha.,21-triol-3,20-dione 21-O-glucosyluronamide (m. 259-60.degree.), pregna-1,4-diene-17.alpha.,21-diol-3,11,20-trione 21-O-glucosyluronamide (m. 257-8.degree.), and pregna-1,4-diene-11.beta.,17.alpha.,21-triol-3,20-dione 21-O-glucosyluronamide [m. 253-4.degree. (decompn.)]. The compds. are useful as **antirheumatic** drugs.

IT Steroids

(21-(glucuronamidosyloxy) derivs.)

IT Glucosiduronamide, 17-hydroxy-3,11,20-trioxopregna 1,4-dien-21-yl
 Glucosiduronamide, 2-(dimethylamino)ethyl N,N-dimethyl-21-yl
 Pregn-4-ene-3,11,20-trione, 21-(glucuronamidosyloxy)-17-hydroxy-
 Pregn-4-ene-3,20-dione, 21-(glucuronamidosyloxy)-11.beta.,17-dihydroxy-
 Pregn-4-ene-3,20-dione, 21-(glucuronamidosyloxy)-17-hydroxy-
 Pregna-1,4-diene-3,11,20-trione, 21-(glucuronamidosyloxy)-17-hydroxy-
 Pregna-1,4-diene-3,20-dione, 21-(glucuronamidosyloxy)-11.beta.,17-dihydroxy-

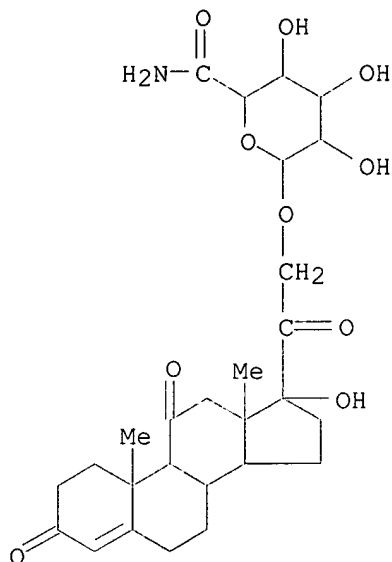
IT 104644-57-7, Glucosiduronamide, 17-hydroxy-3,11,20-trioxopregna-4-en-21-yl 104644-58-8, Glucosiduronamide, 11.beta.,17-dihydroxy-

3,20-dioxopregna-1,4 dien-21-yl 106766-25-0, Glucosiduronamide,
17-hydroxy-3,20-dioxopregn-4-en-21-yl
(prepn. of)

IT 104644-57-7, Glucosiduronamide, 17-hydroxy-3,11,20-trioxopregn-4-
en-21-yl 104644-58-8, Glucosiduronamide, 11.beta.,17-dihydroxy-
3,20-dioxopregna-1,4 dien-21-yl
(prepn. of)

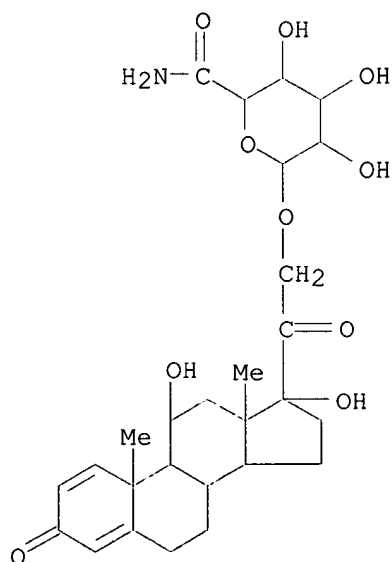
RN 104644-57-7 HCAPLUS

CN Glucosiduronamide, 17-hydroxy-3,11,20-trioxopregn-4-en-21-yl (7CI) (CA
INDEX NAME)



RN 104644-58-8 HCAPLUS

CN Glucosiduronamide, 11.beta.,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl
(7CI) (CA INDEX NAME)



AN 1961:23889 HCAPLUS
DN 55:23889
OREF 55:4748e
TI **Allergic** reactions induced by simple chemical compounds. VI
AU Ishikawa, Mitsuteru
CS Jikeikai School Med., Tokyo
SO Jikeikai Med. J. (1958), 5, 96-122
DT Journal
LA Unavailable
CC 11G (Biological Chemistry: Pathology)
AB A review with 93 references.

=> fil hcaold

FILE 'HCAOLD' ENTERED AT 14:32:26 ON 15 DEC 2002
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

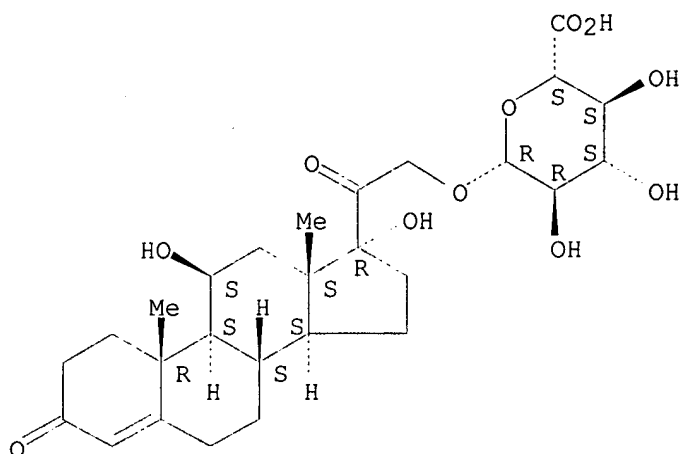
This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d all hitstr 1105

L105 ANSWER 1 OF 1 HCAOLD COPYRIGHT 2002 ACS
AN CA55:4748e CAOLD
TI 17-hydroxy corticosteroids in kidney diseases
AU Karl, H. J.; Forbica, M.
TI **allergic** reactions induced by simple chem. compds. - (VI)
AU **Ishikawa, Mitsuteru**
IT 7301-54-4
IT 7301-54-4
RN 7301-54-4 HCAOLD
CN .beta.-D-Glucopyranosiduronic acid, (11.beta.)-11,17-dihydroxy-3,20-dioxopregn-4-en-21-yl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 13:09:05 ON 15 DEC 2002)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 13:09:20 ON 15 DEC 2002

E STRAKAN/PA,CS
L1 11 S E3-E10
E HOLICK M/AU
L2 475 S E3-E11
E RAMANATHAN H/AU
L3 22 S E3,E4
L4 6 S L1 AND L2,L3
L5 22 S L1-L3 AND STEROID?/SC,SX
L6 4 S L5 NOT ?VITAMIN?
E US2001-41676/AP,PRN
E US2001041676/PN
L7 1 S E3
L8 1 S L7 AND L1-L7
SEL RN

FILE 'REGISTRY' ENTERED AT 13:13:29 ON 15 DEC 2002

L9 13 S E1-E13
L10 5 S L9 AND NR>=5
L11 4 S L10 NOT C24H31FO6
L12 STR
L13 50 S L12 CSS
L14 5950 S L12 CSS FUL
SAV L14 FONDA759/A
L15 STR L12
L16 3653 S L15 CSS FUL SUB=L14
SAV L16 FONDA759A/A
L17 227 S L16 AND OC5/ES
L18 3 S L16 AND OCOC2-OC5/ES
L19 131 S L17 AND 1/NC
L20 42 S L19 AND (N OR S OR P OR SI)/ELS
L21 17 S L20 AND (C41H57NO8 OR C37H54FNO12S OR C56H59NO19 OR C43H66FNO
L22 25 S L20 NOT L21
L23 89 S L19 NOT L20
L24 19 S L23 AND (C30H39FO8 OR C28H36O8 OR C26H37FO6 OR C26H38O6 OR C2
L25 70 S L23 NOT L24
L26 98 S L18,L22,L25

L27 95 S L16 AND OC4/ES
 L28 44 S L27 AND NC>=2
 L29 51 S L27 NOT L28
 L30 96 S L17 NOT L19
 L31 5 S L30 AND (H3N OR BA/ELS OR H2O)
 L32 23 S L30 AND NA/ELS
 L33 21 S L32 NOT (MXS/CI OR C29H38O8)
 L34 124 S L26,L31,L33
 L35 3344 S L16 NOT L17-L34
 L36 STR
 L37 2 S L36 FUL SUB=L35
 L38 STR L36
 L39 0 S L38 FUL SUB=L35
 L40 STR L36
 L41 1 S L40 FUL SUB=L35
 L42 STR L36
 L43 0 S L42 FUL SUB=L35
 L44 3 S L37,L39,L41,L43
 SAV L44 FONDA759B/A
 SAV L34 FONDA759C/A

FILE 'HCAOLD' ENTERED AT 14:01:06 ON 15 DEC 2002

L45 17 S L34
 L46 0 S L11
 SEL AN L45
 EDIT E14-E30
 EDIT E14-E30 /AN /OREF

FILE 'HCAPLUS' ENTERED AT 14:02:31 ON 15 DEC 2002

L47 28 S E14-E30
 SEL DN 3 5 7 9 11 14 17 19 21 22 24 26
 L48 12 S L47 AND E31-E42
 SEL DN 8
 L49 1 S E43
 L50 11 S L48 NOT L49
 L51 17 S L47 NOT L50
 L52 6 S L11
 L53 50 S L34
 L54 50 S L52,L53
 L55 1 S L54 AND L1-L3
 L56 50 S L54 AND (PY<=2000 OR PRY<=2000 OR AY<=2000)
 L57 49 S L54 NOT L55
 L58 7 S (L11 OR L34) (L) (THU OR BAC OR PAC OR DGN OR AGR OR COS OR DMA
 L59 17 S L54 AND (?INFLAM? OR IMMUN?(L)RESPON? OR ADRENAL(L)INSUFF? OR
 E ADREN/CT
 L60 2998 S E10-E21
 E E9+ALL
 L61 29468 S E3+NT
 E E8+ALL
 L62 6512 S E3+NT
 E ADDISON/CT
 L63 460 S E5
 E E5+ALL
 L64 460 S E5+NT
 E CONGENITAL HYPERPLASIA/CT
 E E4+ALL
 L65 341 S E2
 E INFLAMMATION/CT
 L66 23441 S E3-E18
 E E3+ALL
 L67 71073 S E2+NT
 L68 10697 S E37+NT
 E E36+ALL

L69 47496 S E4,E5,E3+NT
E IMMUNE SYSTEM/CT
E E4+ALL
L70 4605 S E2
E EYE DISEASE/CT
E E4+ALL
E E2+ALL
L71 23320 S E3+NT
L72 56794 S E99+NT
E BRAIN EDEMA/CT
L73 1 S E3
E E3+ALL
L74 849 S E2
E SPASM/CT
E E17+ALL
E CONVULSION/CT
L75 502 S E8
L76 379 S E9
E E3+ALL
L77 1661565 S E OR E2+NT
E ALLERGY/CT
L78 17012 S E3-E14
E E3+ALL
L79 18673 S E3,E2+NT
E E16+ALL
L80 6368 S E4+NT
L81 349 S E17+NT
E RHEUMATISM/CT
E E3+ALL
L82 1141 S E1
E E2+ALL
L83 20683 S E4,E3+NT
E NEPHROTIC/CT
E E4+ALL
L84 709 S E2
E SKIN DISEASE/CT
E E4+ALL
L85 10923 S E2
L86 1 S E1
E E2+ALL
L87 48885 S E3+NT
L88 6588 S E114+NT OR E145+NT
E RESPIRATORY DISTRESS/CT
L89 2182 S E5-E8
E E4+ALL
L90 3050 S E4+NT
E IMMUNE SYSTEM/CT
E E4+ALL
L91 4605 S E2
L92 9 S L54 AND L60-L91
SEL DN AN 5 6
L93 7 S L92 NOT E1-E6
L94 13 S L58,L59 NOT L92
L95 20 S L55,L93,L94
L96 20 S L95 AND L54-L95
L97 30 S L54 NOT L96
L98 27 S L97 NOT L51
SEL DN AN 3 5 8 9
L99 4 S E7-E18 AND L98
L100 24 S L96,L99
L101 13 S L51 NOT L100
L102 1 S L101 AND ALLERG?
L103 25 S L100,L102

L104 35 S L51,L54 NOT L103
 SAV L104 FONDA759D/A

FILE 'HCAOLD' ENTERED AT 14:32:10 ON 15 DEC 2002
L105 1 S ALLERG?/TI AND ISHIKAWA ?/AU AND L45

FILE 'HCAOLD' ENTERED AT 14:32:26 ON 15 DEC 2002